Examining the Role and Plasticity of Cognitive Biases in Adolescent Pain Experiences



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A thesis submitted for the degree of
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Abstract

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Acute pain is a common experience in childhood and adolescence. However, a significant minority of young people experience persistent, chronic pain that impairs their physical, emotional, and social functioning. Research presented in this thesis examines cognitive and affective factors in the emergence and chronicity of pain experiences in adolescence. In Chapters Two and Three, data are presented showing that, in community samples of adolescents, associations between pain-related attention biases and pain-related anxiety and catastrophizing are moderated by adolescents' ability to exert effortful attention control. Attention control is also shown to moderate associations between anxiety and tolerance of experimentally-induced pain. In Chapter Four, Attention Bias Modification (ABM) training methodology is used to investigate the plasticity and causal impact of pain-related attention biases in adolescents with chronic pain. Findings indicated that ABM, compared with placebo or no training, did not manipulate attention bias or attention control, nor did it significantly impact pain symptoms, pain catastrophizing, anxious and depressive symptoms, or physical functioning. In Chapters Five and Six, a novel measure of pain-related interpretation bias was developed; the Adolescent Interpretations of Bodily Threat (AIBT) task. Data from this task indicated that, in a community sample of adolescents, the tendency to interpret ambiguous information as indicative of pain and bodily threat mediated associations between pain catastrophizing and recent pain experiences. Additional data indicated that adolescents with chronic pain were less likely to believe benign interpretations of ambiguous bodily-threat information than healthy controls. This interpretation pattern was associated with increased disability among adolescents with chronic pain. In summary, studies in this thesis support the contribution of cognitive biases to pain experiences in adolescence, although the efficacy of ABM was not supported. Further studies investigating the interaction of attention bias and control, as well as biased interpretations of bodily threat, may be particularly useful going forward.

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Declaration

This thesis comprises work conducted by Lauren C Heathcote for the degree of Doctor of Philosophy from the University of Oxford. Four of the chapters contain content that is published or currently under review in peer-reviewed journals, but these chapters have been edited and formatted for this thesis. Recruitment and data collection for Chapter Three was completed at the University of Ghent, Belgium (Lauren was situated in Belgium for these stages). Studies presented in all other chapters were carried out in and around Oxford. Lauren C Heathcote has led all work included in this thesis.

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Chapter 1

1

Introduction

"The health of a nation is largely a reflection of the past and present health of its children"

Forrest and Riley (2004, p.155)

1.1. The Problem of Pain in Youth

1.1.1. The problem of pain in youth

Pain is a common experience in childhood and adolescence (Perquin et al., 2000). Young people frequently report pain following an acute injury (e.g., falls) as well as headaches, stomachaches, and musculoskeletal pains. For most young people, these pains are short-lived, uncomplicated, and have little impact on daily functioning. However, a significant minority of children and adolescents report persistent pain that continues for days, months, or years. It is estimated that up to 37.3% of young people experience recurrent or continuous pain for more than three months (Huguet & Miró, 2008; Perquin et al., 2000), at which point it is described as 'chronic' (Merskey & Bogduk, 1994). Whilst this chronic pain can be mild and relatively non-invasive, around 5.1% of youth report moderate or severe chronic pain that significantly interferes with their daily lives (Huguet & Miró, 2008). It is these young people for whom help is likely most needed to treat pain and associated

problems (Palermo, Valrie, & Karlson, 2014). The research presented in this thesis was conducted to add to the evidence base that may contribute to bettering the lives of these young people.

1.1.2. What is pain, anyway?

Since the time of Descartes, pain has traditionally been discussed within a biomedical model (Chorney, Crofton, & McClain, 2011). This model assumes a one-to-one correspondence between tissue damage, nociceptive input, and pain sensation. On this basis, pain is recognized as a reliable diagnostic marker for tissue damage, and therefore as a useful signal to warn of danger to bodily integrity. The experience of pain is thus expected to promote biomedically-focused problem-solving behavior, for example removing the source of pain, resting the body part to encourage healing, or seeking medical intervention (Eccleston & Crombez, 2007). Within the biomedical model, psychological or behavioural issues arise as a consequence of pain but do not influence the pain experience itself (Chorney et al., 2011). Despite the appealing simplicity of the biomedical model, it is now widely acknowledged that there is great variability in individuals' responses to the same nociceptive input. What's more, many chronic pain conditions have seemingly little evidence of underlying or continuing tissue damage. Given this counter-evidence, a biopsychosocial perspective of pain has emerged. This perspective highlights the interactions between physiological, psychological, and sociocultural influences on the human experience of pain, and has guided much research on acute and chronic pain in the last decades. In the context of chronic pain, there is currently active research on neurobiological factors (e.g., changes in the nervous system, including central sensitization (Fitzgerald, 2011)), cognitive-affective and behavioural factors (e.g., the role of fear and avoidance in driving pain and disability (Vlaeyen & Linton, 2000)), and sociocultural factors (e.g., the role of communication about

pain (Craig, 2009)). It is arguably at the intersection of these approaches that the greatest leaps in scientific understanding will be made.

In line with the biopsychosocial model, the International Association for the Study of Pain (IASP) defines pain as "an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage" (Merskey & Bogduk, 1994). This working definition highlights the role of physiological, affective, and social influences on pain. This definition, and the broader biopsychosocial model, is used as the guiding framework in this thesis.

1.1.3. Prevalence, impact, and cost of chronic pain in youth

The epidemiology of chronic pain in youth has been well documented over the last decade. Two cross-sectional, population-based studies found that 25% to 37.3% of children and adolescents report chronic pain (Huguet & Miró, 2008; Perquin et al., 2000), and 5.1% report moderate or severe chronic pain (Huguet & Miró, 2008). This is in line with prevalence rates reported in adult samples (Johannes, Le, Zhou, Johnston, & Dworkin, 2010). Children and adolescents may experience chronic pain related to injury (e.g., burns) or to an underlying disease process (e.g., cancer, arthritis). However, pain can also be the chronic condition itself (e.g., complex regional pain syndrome) and can occur without any identifiable injury or disease (e.g., fibromyalgia, functional abdominal pain) (Palermo et al., 2014). Indeed, pain is considered by some as a disease in its own right (Siddall & Cousins, 2004). Whilst pain is considered chronic after three months, data suggest than many young people experience pain as a longer-term condition. In a community sample, 54% of youth with musculoskeletal pain continued to experience pain at a one-year follow-up (El-Metwally, Salminen, Auvinen, Kautiainen, & Mikkelsson, 2004). In a clinical sample, 62% of youth with chronic pain continued to report pain up to six years later (Martin, McGrath,

Brown, & Katz, 2007). The most common recurrent pain complaints in youth are headache (*Mdn* = 23%) and abdominal pain (*Mdn* = 12%) (King et al., 2011). Musculoskeletal pain is also commonly reported by young people, with estimated weekly prevalence rates ranging from 8.5% (Brun Sundblad, Saartok, & Engstrom, 2007) to 25% (Smedbråten, Natvig, Rutle, & Bruusgaard, 1998). Many youth also report multiple, widespread pains (King et al., 2011). Chronic pain is more common in girls, however this sex difference depends on pain location, with headache and abdominal pain more frequently reported by girls, and lower limb pain more frequently reported by boys (Huguet & Miró, 2008).

Severe chronic pain in youth, often classified as pain with a severity rating of at least five out of ten (on a visual analogue scale), and experienced at least once a week (Huguet & Miró, 2008), is associated with substantial interference in daily life. This includes interruption in school activities. Indeed, chronic and recurrent pain account for more school absences than any other chronic illness (Palermo, 2000). Youth with chronic pain also report substantial impairment in social development and emotional functioning (Huguet & Miró, 2008). The impact of chronic pain is not limited to the child, but also has significant impact on others in the family unit (Palermo et al., 2014). Parents of youth with chronic pain often report high levels of distress, anxiety, and depression (Eccleston, Crombez, Scotford, Clinch, & Connell, 2004). The impact of chronic pain is also not limited to the childhood years. Many youth with chronic pain continue to report somatic complaints into early adulthood (Christensen & Mortensen, 1975; Kashikar-Zuck et al., 2010), and findings suggest that youth with chronic pain are at increased risk of adult emotional and psychiatric disorders (Hotopf, Carr, Mayou, Wadsworth, & Wessely, 1998; Kashikar-Zuck et al., 2010). Thus, there is a clear need to intervene early.

Paediatric chronic pain is not only costly in terms of its impact on quality of life, but it also entails significant financial costs to individual families and to society. These costs result

from healthcare utilization, out-of-pocket expenses, and parent lost employment and productivity. A preliminary study in the UK found that the familial financial burden of youth chronic pain was £8,027 per year, per youth (Sleed, Eccleston, Beecham, Knapp, & Jordan, 2005). Extrapolating from prevalence rates reported above, it is estimated that 480,000 young people in the UK experience severe chronic pain each year, equating to an annual UK societal cost of £3,840 million (Sleed et al., 2005). A more recent study from the US achieved similar results, with family costs estimated at $11,787 per year, and thus an annual societal cost of $19.5 billion (Groenewald, Essner, Wright, Fesinmeyer, & Palermo, 2014). Research on the causes, consequences, and treatment of chronic pain in youth is needed to reduce this substantial economic burden to families and to society.

1.1.4. Why study adolescence?

Whilst the broader literature discussed above focuses on pain in children and young people, this thesis focuses particularly on the experience of pain in adolescence. Adolescence is broadly defined as the period following the onset of puberty during which a young person develops from a child into an adult (Oxford English Dictionary, 2014). In research on adolescence, although pubertal indicators are sometimes used to identify onset, there is some disagreement as to the stage at which an adolescent reaches adulthood. Nonetheless, studies reported in the current thesis use age as a proxy for adolescence (participants recruited for this thesis were mostly aged 10-18 years old, apart from Chapter Three, for which participants ages 8-9 years were also recruited to increase sample size). Indeed, adolescence may be a key developmental stage associated with the onset of chronic pain. Whilst chronic pain is sometimes reported by younger children, the prevalence of chronic pain rises steeply in later childhood and early adolescence (Perquin et al., 2000).

The impact of chronic pain on the lives of adolescents may also differ to chronic pain in childhood. Adolescence is a time of increased autonomy from parents (Moretti & Peled, 2004), yet the disabling nature of chronic pain can make adolescents reliant on parents later into development. Chronic pain is therefore likely to impact the natural course of emerging independence into early adulthood. In addition, as time spent with family members diminishes in adolescence, peer relationships become critically important (De Lorme, Bell, & Sisk, 2013; E. E. Nelson, Leibenluft, McClure, & Pine, 2005), making peers a newly salient influence for status, identity, and personal experiences. There is growing evidence that chronic pain can interfere with peer interactions and negatively impact peer relationships (Forgeron et al., 2010). Relatedly, peer relationship problems during adolescence have been shown to have significant impact in later life (Bagwell, Newcomb, & Bukowski, 1998), and poor social relationships are recognised as a mortality risk factor comparable to factors such as smoking and obesity (Holt-Lunstad, Smith, & Layton, 2010). Thus, whilst it is important to study chronic pain disorders in both children and adolescents, the unique adolescent developmental period may alter the psychological context in which pain appears, and the experience of chronic pain during adolescence may be particularly impactful on adult functioning (Fales & Forgeron, 2014).

The developmental trajectory of chronic pain is also similar to other psychopathological disorders such as anxiety, which often has its first onset in later childhood and early adolescence (Beesdo, Knappe, & Pine, 2009). Relatedly, there is also a strong association between anxiety and chronic pain in adolescence (King et al., 2011). Indeed, anxiety disorders often co-occur with chronic pain in youth (Knook et al., 2011). In addition, some of the psychological factors purportedly involved in the maintenance of both paediatric chronic pain and anxiety disorders are similar in nature. For example, there are similarities between the roles of fear and avoidance in models of paediatric chronic pain (Simons &

Kaczynski, 2012) and paediatric anxiety disorders (Beesdo et al., 2009). Whether anxiety precedes pain or is a consequence of pain is currently unclear given the lack of prospective studies. However, the significant overlap between anxiety and chronic pain in adolescence suggests that a transdiagnostic approach may be particularly informative for understanding the etiology of chronic pain disorders at this developmental stage. The studies presented in this thesis are largely informed by this transdiagnostic approach, in particular by focusing on cognitive-affective processes that may be shared between paediatric chronic pain and anxiety disorders, and by employing methodologies that have previously been used in the study of adolescent anxiety. Throughout this thesis, I will draw from findings in the paediatric anxiety literature to justify theoretical decisions and methodological choices in study design, and to discuss the broader relevance of findings for adolescent health.

1.2. Cognitive and Affective Influences on Pain

1.2.1. Affective influences on pain

The IASP definition of pain (Merskey & Bogduk, 1994), and the biopsychosocial model, recognise that pain is not only a sensory experience, but also an emotional one. At the 'state' level, emotion and mood are contributing factors in many psychological models of chronic pain aetiology. In particular, fear, negative affect, and anger are argued to promote avoidance of pain following initial injury, thus driving a vicious cycle of deconditioning, disability, and increased pain (Peters, 2015). On the other hand, positive emotions are argued to provide a protective role and to reduce pain sensitivity (Finan & Garland, 2015). At a 'trait' level, anxiety and depression are suggested to be involved in the amplification and chronification of pain, as well as to impact associated functioning, disability, and quality of life. Interestingly, the emotional experience of pain appears to be somewhat different in

young people than in adults (Chorney et al., 2011). Whilst depression is most commonly comorbid with pain in adults (Gatchel, 1996), anxiety appears to be the most commonly comorbid condition in youth (Campo et al., 2004; Chorney et al., 2011; Lipsitz et al., 2005). Given these findings, and given that anxiety-related factors form the focus of research presented in the current thesis, the role of fear and anxiety in pain are discussed in more detail below.

One of the most influential psychological models of chronic pain, the fear-avoidance model (FAM) (Leeuw et al., 2007; Vlaeyen & Linton, 2000, 2012), places anxiety-related factors (notably fear and avoidance) at the centre of pain chronicity. According to the FAM, if an acute injury is followed by fear of pain and fear of re-injury, the individual is likely to avoid further pain and thus further activity. Persistent inactivity can, in turn, lead to a cycle of deconditioning, disability, and distress, and subsequently to increased pain intensity (Peters, 2015). There is growing data from adult populations to support the FAM. For example, experimental research has shown that generalised and pain-related anxiety can increase pain sensitivity (George, Dannecker, & Robinson, 2006; Horn, Alappattu, Gay, & Bishop, 2014; Robinson, Bialosky, Bishop, Price, & George, 2010). Correlational studies have corroborated associations between pain-related fear, pain intensity, disability, and distress in patients with chronic musculoskeletal pain (Peters, Vlaeyen, & Weber, 2005; Zale, Lange, Fields, & Ditre, 2013). Prospective studies have also supported a role of pain-related fear in predicting the transition from acute to chronic pain, and the emergence of long-term disability (see (Peters, 2015) for a useful summary of prospective studies). Whilst the majority of this research has been conducted in adults, the FAM model has also recently been extended to the paediatric context (Asmundson, Noel, Petter, & Parkerson, 2012). The Paediatric FAM also acknowledges the role of young people's fear and anxiety in driving disability and pain chronicity, whilst additionally identifying roles of caregiver psychological responses and

pain-management behaviours in further enforcing the young person's maladaptive responses to pain.

The most comprehensive examination of the FAM in a paediatric sample to date was conducted by Simons and colleagues (Simons & Kaczynski, 2012). Their cross-sectional and prospective data confirmed that the FAM was an excellent fit (using structural equation modelling) in predicting young patients' levels of functional disability. Interestingly, when examining differences between child and adolescent patients, they found that duration of pain contributed more to the model of younger children, while pain-related fears were more influential for adolescent participants, again supporting the examination of anxiety-linked processes in adolescent populations, and suggesting that the maintenance of adolescent pain may be distinct to that of child pain. The FAM has thus been a useful guiding framework for adult pain research to date, and there is emerging evidence that it may also contribute to our understanding of chronic pain in youth. It is important to note, however, that the FAM, and other psychological models of chronic pain (e.g., (Eccleston & Crombez, 1999, 2007; Vlaeyen & Linton, 2000)) comprise not only affective components, but also cognitive factors.

1.2.2. Cognitive influences on pain

The role of cognition in the experience of pain has received much attention since the advent of the biopsychosocial model. Like affective factors, cognitive factors are argued to modulate the experience of pain as well as the development of pain-related outcomes such as disability. The most studied cognitive processes in relation to pain are attention and appraisal. I will now consider each of these briefly in turn before considering the specific construct of 'cognitive bias', which is more central to all studies presented in this thesis.

Pain functions to capture attention, motivating avoidance of potential bodily harm (Eccleston & Crombez, 1999). It is perhaps the most salient cue of danger for both human

and non-human animal species, and thus its attention-grabbing nature is argued to have involved due to adaptability for survival. It should therefore be acknowledged that attentional capture by pain is arguably an adaptive response in acute pain situations. In broad terms, increased attending towards pain is argued to bring it into focal awareness, increasing its saliency and therefore its intensity and interruptive impact on pain-related goals (e.g., avoidance of potential or further harm). Directing attention away from pain, on the other hand, is proposed to decrease its saliency and therefore its intensity, reinforcing attention to non-pain related goals (e.g., searching for food, engaging in social activities). Numerous studies have supported a role of attention in modulating the experience of pain. Studies in both adults and youths have generally found that distraction (e.g., by completing a concurrent non-pain task) decreases pain, whilst focus on pain increases it (see (Peters, 2015) for a useful summary of findings). As expected, studies also find that acute pain interrupts the performance of adults on a range of attention-demanding tasks (Moore, Keogh, & Eccleston, 2012). Interestingly, the majority of research on the role of attention in child and adolescent pain is within the context of cognitive bias, and thus these studies will be discussed in the later section on attention bias.

Once pain has captured attention, it demands interpretation. The role of appraisal has received much consideration under the biopsychosocial model, with studies focusing on the individual's interpretation of the meaning of pain, as well as its causes and consequences. There is growing interest in the protective role of optimism in the experience of pain (Hanssen, Peters, Vlaeyen, Meevissen, & Vancleef, 2013), although this research has yet to be well applied to the paediatric context. Instead, one particular (negative) appraisal process has dominated both adult and paediatric research in this area: pain catastrophizing. Pain catastrophizing is defined as "an exaggerated negative mental set brought to bear during actual or anticipated pain experience" (Michael J L Sullivan et al., 2001). It comprises three

core components; magnification, rumination, and helplessness. Catastrophizing is also a core component of the FAM. In fact, in the FAM, catastrophizing is argued to be a precursor to pain-related fear, thus acting as the fundamental psychological process that drives affective responses, pain chronicity, and disability (Vlaeyen & Linton, 2000). In adult samples, pain catastrophizing has been related to increased sensitivity to experimental pain, and prospective studies have supported a role of catastrophizing in the transition from acute to chronic pain (see (Quartana, Campbell, & Edwards, 2009; Michael J L Sullivan et al., 2001) for reviews summarizing this evidence). Catastrophizing has also received a great deal of attention in the study of child and adolescent pain populations. Pain catastrophizing has been found to be significantly higher in youth with chronic pain compared to healthy samples (Vervoort et al., 2008). Correlational studies have also revealed positive associations between pain catastrophizing and pain severity, as well as disability, in schoolchildren (Vervoort, Goubert, Eccleston, Bijttebier, & Crombez, 2006) and youth with chronic pain (Tran et al., 2015; Vervoort et al., 2006). Interestingly, two studies also revealed that catastrophizing is independently associated with pain experiences and related disability beyond the effects of anxiety (Tran et al., 2015) and negative affectivity (Vervoort et al., 2006), suggesting that these processes may be less interconnected than the FAM model would predict.

Whilst I have considered affective and cognitive processes separately above, it is also important to note that there is considerable overlap between these factors (indeed some argue that affect is a form of cognition (Duncan & Barrett, 2007)). The interconnections between affect and cognition are well exemplified by research in the area of ‘cognitive bias’, to which we now turn. Given that the phenomenological study of cognitive bias in chronic pain arguably has its roots in the study of psychopathology, I will first discuss the broader history of research on cognitive biases before considering their role in pain more specifically.

1.2.3. Cognitive bias and threat perception as a transdiagnostic process

Cognitive bias is a feature of most psychopathological models of behaviour (Mathews & MacLeod, 2005). At the heart of these models is the core assumption that affective and cognitive processes interact to enhance and facilitate the perception of threat in our internal and external environments. Although cognitive biases have been applied to the study of pain for over a decade, many of these studies have their roots in the literature on emotional disorders, where cognitive biases have been most thoroughly investigated. In short, the working hypothesis for most cognitive-affective models of psychopathology is that negative cognitive biases are a contributory and maintaining cause of emotional disorders (Mathews & MacLeod, 2005). Research has focused on biased cognition in three core areas: attention, interpretation, and memory. In short, biased attending to threatening information, biased interpretation of ambiguous information as threatening, and biased memory for threatening information, are all argued to contribute to the development and maintenance of emotional disorders such as anxiety and depression. As opposed to the study of more general attention and appraisal processes discussed above, the relatively specific conceptualisation of attention, interpretation, and memory biases within this field, at least in terms of methodology used to study these biases, has led to a more unified wealth of evidence. The two processes of central consideration in this thesis are attention bias and interpretation bias, which I will focus on in more detail now. However, I will consider the relevance of the research presented in this thesis for research on memory bias in the final chapter.

Attention bias is often defined as the habitual selection of threat-related information over neutral or benign information. Interpretation bias is defined as the tendency to interpret ambiguous information, that is, information with multiple possible appraisals, in a negative or threat-related way. It is broadly argued that habitually attending to negative, threatening information, and interpreting ambiguous information in a negative, threatening manner, will

potentiate perceptions of threat and danger in the environment. In turn, this is argued to increase negative emotional experiences, and thus also increase vulnerability to psychopathology. To date, theory on the role of attention and interpretation biases in emotional disorders has received support from observational and experimental studies. However, these models have not gone unchallenged, both in terms of their theoretical premises as well as the methodology most commonly used to study biased cognition. These challenges and limitations will again be more thoroughly considered in the final chapter of this thesis.

Regardless of limitations, it is clear why models of cognitive bias have made their way into the study of pain. First, as discussed above, cognitive and affective factors have already been identified to play a role in the human experience of pain and pain-related outcomes. Second, also discussed above, high comorbidity between emotional disorders and chronic pain, in both adult and paediatric populations, indicate that a transdiagnostic approach to studying aetiology, as well as intervention, may be beneficial. Third, there is a clear unifying construct across models of cognitive bias in pain and psychopathology; the detection and perception of threat. Although there may be differences in the content of the threat, for example, whether it is external to the individual (e.g., negative social cues in the case of social anxiety disorder), or internal to the individual (e.g., physiological sensations such as respiration in the case of panic disorder, and painful sensations in the case of chronic pain), the processes that facilitate and enhance threat perception may be similar across disorders. Thus, methodologies used to study threat perception in the anxiety and depressive disorders could be usefully applied to the study of chronic pain. Moreover, many of the principal questions in the literature on cognitive bias and emotional disorders may also be relevant for our understanding of cognitive-affective processes in pain. One of these core questions regards the specificity of biases in terms of cognitive process, content of stimuli,

and type of disorder. For example, whilst attention bias has been most identified within the anxiety disorders, memory biases have been more identified in depressed samples (Mathews & MacLeod, 2005). Additionally, central to most models of cognitive bias in psychopathology is the hypothesis that cognition will be biased particularly towards information that is relevant to the individual's disorder (the content-specificity hypothesis (A. T. Beck, 1976)). Thus, we would expect to find biased processing of pain-related information, but not, for example, spider-related information, in patients with chronic pain, and vice versa for patients with spider phobia.

The research presented in this thesis was designed and conducted within a transdiagnostic understanding of cognitive bias and threat perception. I will now turn to consider the history of research on cognitive bias and pain. I will first summarise the key theoretical models that have guided empirical studies in this area over the last two decades, before reviewing experimental findings. Given that the majority of research on cognitive bias and pain to date has been conducted in adults, I will first discuss findings from the adult literature, before moving to consider research in paediatric samples.

1.3. The Role and Plasticity of Cognitive Bias in Pain

1.3.1. Theoretical models implicating cognitive biases in chronic pain

Cognitive-affective processes have long been considered important in the perception of bodily sensations in general (Cioffi, 1991; Pennebaker, 1982), and in the experience of pain in particular (Eccleston & Crombez, 1999; Pincus & Morley, 2001). Since the turn of the century, a number of psychological models have been proposed that implicate a specific role of cognitive biases in the aetiology of chronic pain. One of the first models was the FAM (Vlaeyen & Linton, 2000), described in detail above. Around the same time, Eccleston and

Crombez (Eccleston & Crombez, 1999) presented another model with cognitive-affective processes at its heart. In their Cognitive-Affective Model of the Interruptive Function of Pain, Eccleston and Crombez argue that the most defining features of pain is that it interrupts attention, distracts from current task engagement, and is difficult to disengage from. Thus, they argue for a redefinition of chronic pain as 'chronic interruption' (Eccleston & Crombez, 1999). Under this framework, biased attention towards pain over competing demands is evolutionarily primitive, and can be considered normative. However, in line with a transdiagnostic approach, it is the perception of pain as threatening that is argued to mediate interruption by pain, and thus to drive maladaptive functioning and responding. In line with the literature on cognition in pain discussed above, one such process that moderates the determination of threat is whether the person catastrophizes about pain. Other suggested moderators are the intensity, novelty, and predictability of the pain, as well as the individual's level of somatic awareness (Eccleston & Crombez, 1999). Thus, feature-specific and individual-difference factors are proposed to contribute, and interact, to determine the ability for pain to capture attention.

Two years after Eccleston and Crombez's model, Pincus and Morley presented a new framework that considered more specifically the roles of cognitive biases as they have been described and studied within experimental psychopathology. Their Schema Enmeshment Model of Pain (SEMP) (Pincus & Morley, 2001) draws heavily on schema theory, and predicts that if an individual holds a specific schema, broadly defined as an organized set of beliefs, s/he will selectively filter schema-congruent information at all stages of processing. The SEMP proposes that attention and interpretation biases in chronic pain are the result of overlap between three schemas: pain, illness, and self. Like Eccleston and Crombez's model of interruption, the SEMP proposes that biased cognitive processing of pain-related information is primarily normative and adaptive. However, they argue that the enmeshment

of pain and illness schemas with the self-schema will serve to enhance cognitive biases towards pain and thus to maintain and exacerbate distress and illness behaviour in patients with chronic pain (Pincus & Morley, 2001).

Later that decade, Eccleston and Crombez proposed a new model of chronic pain, the Misdirected Problem-Solving Model (Eccleston & Crombez, 2007). In this model, attentional interruption by pain remains the precipitating factor. However, the process driving individual differences in response to pain is, in this model, problem-solving behaviour. In particular, Eccleston and Crombez (Eccleston & Crombez, 2007) argue that framing chronic pain in biomedical terms will result in problem-solving behaviour directed at biomedical solutions. When no biomedical solution is available, as is often the case in chronic pain disorders, suffering and disability will ensue. Whilst the core component of this model is thus behavioural in nature, a cognitive-affective process is proposed as the core mediator of pain and problem-solving behaviour: worry. Eccleston and Crombez argue that the interruptive nature of pain, especially if persistent, is "an ideal habitat for worry to flourish" ((Eccleston & Crombez, 2007), p.234). Of particular relevance to this thesis, worry is proposed to fuel attention bias towards pain (Eccleston & Crombez, 2007). This attention bias is argued to increase interruption by pain, thus driving further worry and problem-solving behaviour. If the individual maintains a biomedical problem frame, when no biomedical solution is available, the selected problem-solving behaviours will be ineffective, further maintaining worry and attention bias, enforcing a negative perseverance loop (Eccleston & Crombez, 2007).

Building on the models described above, Van Damme and colleagues have more recently proposed that processes of attention, worry, and problem-solving should be considered within a motivational framework (Van Damme, Legrain, Vogt, & Crombez, 2010). Like the models described above, their Motivational Account of Attention to Pain posits attention bias as a

key component of chronic pain aetiology. However, Van Damme and colleagues argue that the degree to which attention is biased towards pain will depend on the individual's concurrent goal pursuit. Like in Eccleston and Crombez's original model of chronic interruption (Eccleston & Crombez, 1999), Van Damme and colleagues (Van Damme et al., 2010) argue that the degree to which attention is captured by pain will depend not only on the sensory characteristics of the pain but also on the psychology of the individual. However, in this case, rather than catastrophizing and somatic awareness as key factors, the degree to which pain is relevant to the individual's pursuit of a concurrent goal is considered most important. In this way, attending to and disengaging from pain are not static mechanisms, but dynamic processes that are modulated by current goal pursuit, allowing wide inter- and intra-individual variability (Van Damme et al., 2010). In particular, Van Damme and colleagues argue that having pain control as a focal goal will enhance attentional processing of pain information, and thus, paradoxically, will increase the interruption of pain on daily life (Van Damme et al., 2010).

Most recently, Todd and colleagues (Todd et al., 2015) proposed a model that is informed by recent prospective and experimental findings in the field of pain-related cognitive bias. Once again, attention bias is central to the model, and is considered the final outcome of a chain of other cognitive-affective processes. Specifically, they argue that an incoming sensory stimulus must first be categorized as pain relevant or pain irrelevant, after which it can be interpreted as threatening or non-threatening (interpretation bias). If a stimulus is determined as pain-relevant and threatening, then an attentional bias, in the form of initial vigilance followed by later avoidance, will arise. Thus, the interpretation of bodily information as pain-related, and threatening, is proposed to drive attention bias towards pain.

Whilst there are clear differences between cognitive-affective models of chronic pain described above, there are also a number of overlapping factors. First, all include a role for

attention bias. Only some models explicitly posit this bias as a normative process (Eccleston & Crombez, 1999, 2007; Pincus & Morley, 2001), however in all models, it is considered maladaptive. Second, all models propose associations between attention bias and other cognitive and affective factors, suggesting that these others factors drive further attention bias. However, the cognitive-affective factors that are proposed to drive attention bias differ somewhat between models. Factors include fear (Vlaeyen & Linton, 2000), worry (Eccleston & Crombez, 2007), catastrophizing (Eccleston & Crombez, 1999), interpretation bias (Pincus & Morley, 2001; Todd et al., 2015), and goal-pursuit (Eccleston & Crombez, 2007; Van Damme et al., 2010), with some factors overlapping more so (e.g., worry and catastrophizing) than others. Despite these differences, another factor that unites all models is the perception of threat. Whether this is the categorization of pain as threatening to bodily integrity (Todd et al., 2015) or as threatening to current goal pursuit (Van Damme et al., 2010), threat-related interpretations of pain and pain-related information are argued to drive attention bias and maladaptive pain outcomes. Taken together, we can draw four key hypotheses from cognitive-affective models of chronic pain:

1) Individuals with chronic pain will display an attention bias towards pain and pain-related information

2) Individuals with chronic pain will interpret ambiguous pain-related and bodily information in a negative, threatening way

3) Fear, worry, and catastrophizing about pain will be associated with increased attention and interpretation biases for pain-related information

4) Attention and interpretation biases will be associated with more negative pain experiences and maladaptive behavioural outcomes

In the next section of this introduction I will summarise empirical studies that have been guided by, and conducted to verify, the theoretical models described above.

1.3.2. Attention bias in adult pain: cross-sectional studies

A number of empirical studies have been conducted in the last two decades on cognitive biases in adult pain populations. The majority of these studies are on attention bias, and three meta-analyses have summarised cross-sectional findings to date. First, Roelofs and colleagues (Roelofs, Peters, Zeegers, & Vlaeyen, 2002) summarised early studies using the modified Stroop paradigm as a measure of selective attention towards pain-related stimuli in adult chronic pain patients. In the modified Stroop, pain-related and neutral words are presented in different colours, and participants are required to name the colour of each word. An attention bias towards pain is indexed by a relative slowing of colour naming for pain-related words compared to neutral words. The meta-analysis pooled data from five studies, and revealed a significant attention bias for both sensory and affective pain words in adult chronic pain patients compared to healthy controls. Thus, the early literature indicated that adult chronic pain patients do display an attention bias towards pain, thus supporting cognitive-affective models. However, some have expressed doubts over the use of the modified Stroop as a measure of attention bias, suggesting that it might better reflect general interference rather than selective attention (Roelofs et al., 2002). Thus, more recent studies have moved towards using visual probe paradigms as an alternative measure of attention bias.

Visual probe paradigms, often referred to as the ‘dot-probe task’, are the most widely used measure of attention bias in pain populations. The affective dot-probe task was originally developed by Macleod and colleagues (MacLeod, Mathews, & Tata, 1986) for the study of anxiety-linked attention bias. In this computerised task, participant response times are recorded to a series of visually presented stimuli. Following an initial fixation point, each

trial presents a pair of stimuli at spatially distinct locations on the screen (e.g., above or below the fixation point). In the pain literature, one stimulus is pain-related (e.g., a pain word or facial expression) and another is neutral. After a specified amount of time (e.g., 500ms), the stimuli are removed from the screen, and one stimulus is replaced by a visual probe (e.g., a dot). An attention bias towards pain is indexed by a relative slowing of response times to identify the probe when it appears away from the pain stimulus (i.e., behind the neutral stimulus) as opposed to behind the pain stimulus. Unlike the modified Stroop paradigm, the dot-probe task is argued to measure spatially selective attention. In addition, the presentation of stimulus pairs for shorter versus longer lengths of times are proposed to index relatively early (e.g., presentation times ≤ 500ms) or later (e.g., presentation times ≥ 1250ms) stages of attentional processing. Schoth and colleagues (Schoth, Nunes, & Liossi, 2012) performed the first meta-analysis on dot-probe studies in adults with chronic pain. They identified ten studies, of which seven used sensory and/or affective pain words as stimuli, and three used pain-related images (facial expressions or headache images). Five of the studies presented stimulus pairs for a single presentation time (300ms or 500ms), whilst the other five studies presented stimulus pairs for two presentation times (500ms and 1250ms). Taken together, Schoth and colleagues (Schoth et al., 2012) found that adult patients with chronic pain demonstrated significantly greater attention bias towards pain-related information compared to healthy, pain free controls. These findings remained significant when examining studies using shorter and longer stimulus presentation durations separately, suggesting that adult chronic pain patients demonstrate attention biases for pain-related information at both early and later stages of attentional processing. Interestingly, though, effect sizes were larger for stimuli presented for longer stimulus durations, indicating that attention biases are more pronounced during later stages of attentional processing – suggestive of biases in the voluntary use of attention.

One year after the meta-analysis by Schoth and colleagues (Schoth et al., 2012), Crombez and colleagues (Crombez, Van Ryckeghem, Eccleston, & Van Damme, 2013) conducted another meta-analysis, but with a broader scope. Crombez and colleagues (Crombez et al., 2013) pooled data from both acute and chronic pain groups, as well as studies considering procedural and experimentally-induced pain. They also included data from multiple attention tasks including the modified Stroop, the dot-probe, and spatial cueing paradigms. The authors identified 50 studies, 22 of which used the modified Stroop, 23 of which used the dot-probe, and 6 of which used the spatial cueing task (one study used both the modified Stroop and the dot-probe on the same participants). Taken together, Crombez and colleagues (Crombez et al., 2013) found a small but significant effect of attentional bias to pain-related information in chronic pain groups, but no evidence of attentional bias to pain-related information in acute, procedural, or experimental pain groups, nor in controls. However, between-groups analyses indicated that there were no significant differences in attention bias between chronic pain groups and control groups. When considering the type of pain-related information presented across studies, however, they found a significant effect size for words representing the sensory quality of pain, but not for words representing the affective quality of pain. In addition, effect sizes for sensory pain words significantly differed between chronic pain and control groups. Moreover, when only considering studies that included sensory pain words, there was a significant difference between chronic pain patients and controls for the dot-probe task. Thus, taken together, Crombez and colleagues (Crombez et al., 2013) found some evidence of attentional bias towards pain-related information in chronic pain groups, but findings were inconsistent and effect sizes were small. However, between-group differences were stronger when considering attention bias for sensory pain stimuli, suggesting that biases may be strongest for information regarding the sensory qualities of pain. Thus, in comparison to the meta-analysis performed by Schoth and

colleagues (Schoth et al., 2012), Crombez and colleagues (Crombez et al., 2013) found evidence that attention biases characterised pain patients only under certain conditions.

Whilst findings from Crombez and colleagues (Crombez et al., 2013) suggest that individuals without chronic pain do not display an attentional bias towards pain-related stimuli, such biases may emerge in individuals who perceive pain as particularly threatening. Indeed, cognitive-affective models predict that if an attention bias plays a causal role in pain chronicity, it is likely to be evident in individuals who are fearful of and catastrophize about pain, as well as those who prioritise pain control as a goal. Interestingly, in an additional analysis, Crombez and colleagues (Crombez et al., 2013) found evidence for an attentional bias towards signals of impending experimental pain (e.g., stimuli that have been paired with pain through conditioning procedures) in healthy samples, suggesting that attentional bias may emerge even in non-pain populations under conditions of high pain-related threat.

Relatedly, a number of studies in the last decade have investigated associations between attention bias for pain-related information and factors such as fear of pain, pain catastrophizing, and goal pursuit in healthy populations. For example, Keogh and colleagues (Keogh, Ellery, Hunt, & Hannent, 2001) provided some initial evidence that healthy individuals with high fear of pain display an attention bias towards pain-related information, whilst those with low fear of pain do not. In addition, Vancleef and colleagues (Vancleef & Peters, 2006) found that pain catastrophizing in healthy individuals was associated with increased attentional interference of experimentally-induced electrical pain on performance of an attentionally-demanding task. More recently, Baum and colleagues (Baum, Schneider, Keogh, & Lautenbacher, 2013) found that individuals high in pain-related fear demonstrated a vigilance-avoidance pattern of attending to pain-related information. However, in contrast, Asmundson and colleagues (Asmundson & Hadjistavropoulos, 2007) found no evidence for

an association between fear of pain and attention bias for pain words in healthy individuals, thus findings are not always replicated.

Regarding goal pursuit, there is preliminary evidence that healthy individuals display an attention bias towards signals of impending pain if they have pain control as a current goal. For example, Notebaert and colleagues (Notebaert et al., 2011) found that individuals who believed that they could control an impending pain stimulus showed an attentional bias towards signals of pain in a computerised visual search task. More recently, Durnez and colleagues (Durnez & Van Damme, 2015) extended these findings, showing that individuals who believed that they could control an impending pain stimulus were better able to detect tactile changes at the pain location than other body locations, indicating an attentional bias for the pain-threatened body location.

Taking studies in patient and healthy populations together, findings to date have provided some evidence that adults with chronic pain display an attention bias towards pain-related information, although effect sizes are small, and appear significant only under certain task conditions (e.g., tasks using sensory pain words). There is also some evidence from healthy populations for associations between attention bias and other pain-related vulnerability factors such as fear of pain and pain catastrophizing, as well as pain-related goals. However, whilst cross-sectional studies are useful in identifying whether biases exist in pain populations, and in the context of pain-related threat, prospective and intervention studies are necessary for examining their causal role in pain experiences. Indeed, whilst an attention bias towards pain-related threat may play a causal role in the onset and/or maintenance of chronic pain disorders, it may alternatively be an epiphenomenon of the pain experience. Thus, I will now discuss studies investigating the causal nature of attention bias in adult pain experiences.

1.3.3. Attention bias in adult pain: prospective and training studies

Cognitive-affective models of chronic pain, as described above, implicate a causal role of attention bias in pain chronicity and associated disability. Yet, few studies to date have employed designs that are able to test this causal hypothesis. Necessary are prospective studies that can determine whether attention biases precede and predict subsequent pain outcomes, although these studies provide only an indirect test of causal associations. Thus, also necessary are experimental studies that directly manipulate attention and can therefore directly test causal associations between attention bias and pain outcomes.

Last year, Todd and colleagues (Todd et al., 2015) presented the first meta-analytic study which pooled data from prospective and experimental (training) studies in this field. All identified studies were in adult populations. Regarding prospective studies, they identified six articles, reporting five studies. Of the five studies, three investigated individuals who were awaiting an acute medical procedure likely to cause pain, one investigated individuals with acute and subacute (low back) pain, and one investigated individuals with chronic pain. Four out of the six studies provided some evidence that attentional biases predicted subsequent pain experiences. Interestingly, though, only one of the studies (Munafò & Stevenson, 2003) identified that an attention bias *towards* pain (words) predicted future pain. In contrast, Lautenbacher and colleagues (Lautenbacher et al., 2009) found that an attention bias *away* from pain (words) was the strongest predictor of postoperative pain. In a paper published one year later, Lautenbacher and colleagues (Lautenbacher et al., 2010) found that an attention bias *towards positive* (non-pain) stimuli predicted whether patients had clinically meaningful pain six months later. Todd and colleagues (Todd et al., 2015) argue that although these latter two findings seem conflicting, they may in fact reflect different facets of the same process. For example, Todd and colleagues (Todd et al., 2015) suggest that a tendency to avoid pain-related stimuli may also result in preferential attending towards non-pain stimuli. These

findings appear somewhat out of line with cognitive-affective models discussed above, which suggest that attending *towards* pain will be primarily maladaptive. However, it should also be noted that the only study finding a causal role of attention bias *towards* pain (Munafò & Stevenson, 2003) used a relatively brief stimulus presentation time (100ms), whilst studies finding a causal role of attention bias *away* from pain used relatively longer stimulus presentation times (500ms), suggesting that a vigilance-avoidance pattern of attending may be most associated with poorer pain outcomes. This hypothesis remains to be directly tested.

In addition to the six prospective studies described above, Todd and colleagues (Todd et al., 2015) also identified six articles, reporting seven studies, in which attention was experimentally manipulated. Five of the studies used Attention Bias Modification (ABM) training that is commonly used in the field of psychopathology (Bar-Haim, 2010). In short, ABM training utilizes computer-based attention training protocols to implicitly modify biased attentional patterns. Studies within the context of pain have used modified versions of the dot-probe task, in which targets consistently appear behind neutral stimuli, and thus away from pain-related stimuli, thereby training the individual to shift their attention away from threat in order to enhance task performance. Two of the ABM studies in the field of pain recruited chronic pain samples, one recruited patients with acute pain, and the remaining two studies recruited unselected samples of university students and examined effects of training on experimentally-induced pain. In the acute pain patient sample, Sharpe and colleagues (Sharpe et al., 2012) found benefits of a single session of ABM on pain outcomes. Specifically, compared to a placebo training group, the group receiving ABM reported less current and average pain, and fewer days in pain three months later. In contrast, neither study with a chronic pain sample found effects of ABM training on pain symptoms (Carleton, Richter, & Asmundson, 2011; Sharpe et al., 2012), although Carleton and colleagues (Carleton et al., 2011) found a trend approaching significance (p = .06). However, both

studies found an effect on other measures such as anxiety sensitivity and disability. Of importance, though, none of the studies in clinical samples have showed that ABM training significantly changed biases, calling into question the mechanism of change in pain, anxiety sensitivity, and disability scores.

Despite that attention biases did not change following training in the acute and chronic pain groups, the two studies in university samples (McGowan, Sharpe, Refshauge, & Nicholas, 2009; Sharpe, Johnson, & Dear, 2015) did demonstrate the predicted change in attention bias following ABM training. These studies also found that after ABM training, participants took longer to register pain (pain threshold) in a cold pressor test (CPT; in which participants submerge their hand in a container of very cold water) compared with the control condition. Only one of the studies showed an impact of ABM on pain intensity, and none showed an impact of ABM on pain tolerance. Todd and colleagues (Todd, Sharpe, & Colagiuri, 2016) argue that these findings are in line with expectations, as attentional processes are arguably more likely to influence how quickly an individual identifies pain, rather than the intensity of the pain or how long the pain can be tolerated for. Interestingly, an additional study with university students has been published since the review by Todd and colleagues (Todd et al., 2015), by the same authors, revealing somewhat conflicting findings. Specifically, Todd and colleagues (Todd et al., 2016) delivered four versions of ABM that differed in training direction. Participants received attention training that was either towards (+) or away from (-) sensory (S) and affective (A) pain words. Thus, there were four ABM training conditions (S+A+, S-A-, S+A-, S-A-). They found that individuals trained *towards affective* pain words had a greater pain threshold but also greater distress at tolerance on the CPT. Training on sensory pain words did not impact pain outcomes, and like in the clinical studies described above, mechanisms of change could not be established, as ABM did not affect attentional bias.

Taken together, ABM studies within the context of pain have provide mixed evidence of the causal impact of attention bias on pain and pain-related outcomes. There is some preliminary evidence that ABM training can impact acute and clinically-relevant pain outcomes, although these findings are only for certain outcomes (disability and anxiety sensitivity), and the mechanism of training effect is not always identified. Given inconsistent findings across studies, there have been recent calls for investigations of other cognitive biases within this context, that may give more reliable findings (Crombez, Heathcote, & Fox, 2015). As the role of threat-interpretations are central to most cognitive-affective models of chronic pain, and as many of these models propose that biased interpretations drive biased attending, some research groups have begun investigating the role and plasticity of interpretation bias in adult pain populations. It is this literature to which I now turn.

1.3.4. Interpretation bias in adult pain

The way in which we interpret pain and cues for pain is proposed to play a central role in the chronicity of pain and the emergence of negative pain-related outcomes in almost all psychological models of pain (e.g., (Aldrich, Eccleston, & Crombez, 2000; Eccleston & Crombez, 1999; Van Damme et al., 2010; Vlaeyen & Linton, 2000). Whilst there are far more published studies on attention bias, there is an emerging literature on the role and plasticity of interpretation biases in pain populations. Studies have typically used self-report measures that are similar to those used in psychopathology populations. For example, participants are presented with ambiguous stimuli that could be appraised in a pain-related or a non-pain related (e.g., benign or neutral) manner. For example, participants may be presented with homophones, which are words that sound the same yet have different spellings and meanings (e.g., pain/pane), or homographs, which are words that have identical spellings yet distinct meanings (e.g., terminal; causing death, airport building). Studies have also used

word-stem completion tasks (e.g., ten___ ; could be completed as ‘tender’ or tennis’). In these paradigms, ambiguous stimuli have at least one pain-related meaning and one benign meaning. Other studies employ ‘ambiguous situation tasks’, in which participants are presented with vignettes of real-life situations which have plausible pain-related as well as benign interpretations. Participants are then asked to generate their own interpretations, or to report whether experimenter-generated interpretations match their own appraisals. More recently, studies have also used computerised cognitive tasks that can measure more spontaneous (on-line) interpretations, for example through measurement of response times.

Earlier this year, Schoth and Liossi (Schoth & Liossi, 2016) pooled available data from chronic pain populations to date, performing meta-analyses to investigate whether or not adults with chronic pain display an interpretation bias for pain-related information. The authors identified six articles, reporting seven studies. The majority of identified studies used single word stimuli (Edwards & Pearce, 1994; McKellar, Clark, & Shriner, 2003; Pincus, Pearce, McClelland, Farley, & Vogel, 1994; Pincus, Pearce, & Perrott, 1996), with only one study using an incidental learning task (Khatibi, Sharpe, Jafari, Gholami, & Dehghani, 2015). In contrast to the inconsistent findings across studies on attention bias, all studies identified by Schoth and Liossi (Schoth & Liossi, 2016) provided some evidence that adult patients with chronic pain display an interpretation bias for pain- and health-related information. Indeed, the meta-analyses revealed that adult chronic pain patients demonstrate significantly more pronounced pain-related interpretations of ambiguous stimuli relatively to healthy controls. In addition, results from the incidental learning task developed by Khatibi and colleagues (Khatibi et al., 2015) provides evidence that adult chronic pain patients display an interpretation bias for pain-related information (in this case, pain facial expressions) even outside of self-report. Another interesting finding that emerged from the meta-analyses is that studies have revealed not only an interpretation bias for ambiguous information relating to

pain specifically, but also to ambiguous information regarding illness, poor health, and bodily threat (Schoth & Liossi, 2016). This finding supports the SEMP model (Pincus & Morley, 2001) which predicts that patients with chronic pain will display biases that are in line with the perception of themselves as ill and in poor health.

As in studies on attention bias, a number of studies have also considered whether a negative pain-related interpretation bias is associated with other pain-related vulnerability factors such as pain catastrophizing and fear of pain, in healthy samples. Interestingly, studies in these healthy samples have tended to use either ambiguous situation tasks, or tasks measuring on-line interpretations (e.g., incidental learning tasks and lexical decision tasks), rather than single word stimuli. Taken together, there is evidence that negative interpretations of ambiguous pain- and health-related information characterise individuals who score highly on measures of pain-related fear and catastrophizing. However, there is some inconsistency regarding which factors are most strongly associated with interpretation bias. For example, Vancleef and colleagues (Vancleef, Peters, & De Jong, 2009) employed a lexical decision task in a community adult sample, and found that the tendency to endorse health-threatening interpretations of ambiguous information was positively associated with fear of pain. However, they also found that this negative interpretation bias was unrelated to levels of pain catastrophizing, as well as levels of anxiety sensitivity (the fear of sensations associated with anxiety) and injury/illness sensitivity, both of which have also been implicated as vulnerability factors for pain chronicity. The non-significant association with catastrophizing is perhaps especially surprising given that both interpretation bias and catastrophizing are appraisal processes. In a different study, this time using an ambiguous situations task, Vancleef and colleagues (Vancleef & Peters, 2008) found that both fear of pain and pain catastrophizing were significantly associated with self-reported negative interpretations of ambiguous bodily symptom information. Interestingly, though, both fear of pain and pain

catastrophizing were also significantly associated with negative interpretations of ambiguous information about panic-related sensations, social events, and general events (e.g., 'you smell smoke'), suggesting that these pain-related vulnerability factors may be associated with a general tendency to interpret ambiguous information in a threatening way. It is worth noting, however, that the strongest associations were between pain catastrophizing and interpretations of ambiguous bodily sensations, suggesting some degree of specificity.

Going beyond bivariate correlations, Keogh and colleagues (Keogh & Cochrane, 2002; Keogh, Hamid, Hamid, & Ellery, 2004) conducted two studies to investigate whether a negative interpretation bias mediated associations between anxiety sensitivity and pain-related outcomes on a cold pressor test (CPT). Both studies found evidence for the mediating effect of interpretation bias, but with some degree of specificity. For example, in the first study, Keogh and colleagues (Keogh & Cochrane, 2002) found a mediating role specifically for the tendency to negatively interpret ambiguous bodily sensations related to panic. In the second study, Keogh and colleagues (Keogh et al., 2004) found that a generalised negative interpretation bias (indexed by a composite score for interpretations of ambiguous bodily sensation, social, and general information) significantly mediated the association between anxiety sensitivity and cold pressor pain outcomes, but only for women. More recently, Khatibi and colleagues (Khatibi, Schrooten, Vancleef, & Vlaeyen, 2014) examined whether high pain catastrophizers demonstrated a negative pain-related interpretation bias using an incidental learning task comprising facial expressions of pain and happiness, as well as morphed facial expressions. As expected, they found that high, but not low catastrophizers were faster to respond to probes that followed morphs that appeared at locations previously predicted by pain facial expressions, indicating that participants interpreted the morphed faces as indicative of pain rather than happiness.

Most recently, Vancleef and colleagues (Vancleef, Hanssen, & Peters, 2016) derived an index of pain-related interpretation bias using an ambiguous health-related homophone priming task, in two separate studies. Like Keogh and colleagues, they also revealed significant associations between a negative interpretation bias and anxiety sensitivity, injury-illness sensitivity, and pain catastrophizing scores in the first study. However, only the association with injury-illness sensitivity remained significant in the second study. Nonetheless, the second study also revealed that a negative interpretation bias was associated with lower tolerance for experimentally-induced heat pain, and that it significantly mediated associations between injury/illness sensitivity and pain tolerance. Thus, taken together, there is relatively consistent evidence across cross-sectional studies that a negative interpretation bias, at least for ambiguous pain-, health-, and bodily-related information, is associated with higher levels of pain-related fear and catastrophizing, as well as anxiety sensitivity, although some studies find associations only with one of these measures. In addition, there is preliminary evidence that a negative interpretation bias mediates the association between anxiety and injury/illness sensitivity, and the experience of experimentally induced pain.

Despite this promising indication for a role of interpretation bias in pain chronicity and pain-related vulnerability, only one study to date has employed a task to investigate more causal associations between these factors. Jones and Sharpe (Jones & Sharpe, 2014) randomly allocated 106 undergraduate students to receive computerised cognitive bias training that encouraged more threatening or more benign interpretations of ambiguous pain-related situations. Like ABM training, the employed Cognitive Bias Modification of Interpretations (CBM-I) has its roots in the study of psychopathology (Grey & Mathews, 2000). As predicted, participants in the threat-training group endorsed more threatening interpretations of ambiguous pain-related information at a post-training test phase, and they hesitated more before immersing their hand in a cold pressor container. Most importantly,

interpretive bias mediated the relationship between training condition and hesitance time, supporting a causal role of interpretation biases for pain avoidance behaviours. Interestingly, though, there was no significant effect of training on pain threshold or tolerance, suggesting that a negative interpretation bias may be associated with avoidance behaviours, but not the pain experience itself, or escape from pain.

Brief summary on cognitive bias and adult pain

In summary, there have been a number of empirical investigations to date into the presence, role, and plasticity of cognitive biases in adult experiences of pain. Most of these studies are cross-sectional, and have either measured attention or interpretation biases in adults with chronic pain, or associations between these biases and other cognitive and affective factors that are implicated in models of chronic pain. A small number of studies have also employed prospective or training designs to better elucidate the causal role of cognitive biases in adult pain experiences, although most of these studies have been conducted for attention biases rather than interpretation biases. When considered together, there is evidence that both attention and interpretation biases characterise adults with chronic pain compared to healthy controls, although findings are more consistent for interpretation biases. Prospective and training studies also suggest that cognitive biases may play a causal role in pain experiences, although effects for studies on attention bias are inconsistent across measures used, and many findings from prospective studies are not in the expected direction. Certainly, findings from prospective studies suggest that measures that capture more dynamic attentional processing will be useful to improve our understanding of causal associations between biases and pain-related outcomes going forward.

Despite a relatively large body of evidence for a role of attention and interpretation biases in adult pain populations, there are far fewer studies in paediatric populations. The

final section of this introduction chapter will discuss published studies on attention and interpretation biases in paediatric samples, before presenting the rationale and key research questions that are central to this thesis.

1.4. Pain-Related Cognitive Biases in Paediatric Populations

1.4.1. Cognitive biases and pain in youth

If cognitive biases are involved in the emergence and early maintenance of chronic pain disorders, we would expect that they should characterise youth with chronic pain, and be associated with pain-related vulnerability in young people. Of particular relevance to this thesis are biases in attention and interpretation. Whilst there are studies on memory bias in child pain populations, these are not central to the studies presented in this thesis, but will be discussed in greater detail in Chapter Seven. As discussed earlier in this chapter, paediatric research has focused on catastrophizing as a primary appraisal process involved in childhood pain. However, no studies to date have investigated pain-related interpretation bias for ambiguous information in youth populations. Thus, the literature reviewed below examines the presence and role of pain-related attention biases in young people.

Only a small number of studies have used experimental tasks to investigate attention biases for pain-related stimuli in youth populations. In total, there are four published studies. Three of these studies compared biases in young people with chronic pain conditions to healthy youth (J. E. Beck et al., 2011; Boyer et al., 2006; van der Veek et al., 2014), and one study examined associations between biases and pain-related individual-difference factors in a sample of healthy youth (Vervoort, Trost, & Van Ryckeghem, 2013). First, Boyer and colleagues (Boyer et al., 2006) examined attention biases for pain-related words and social-threat words in 59 youth (9-17 years) with recurrent abdominal pain (RAP). Participants

completed a modified dot-probe task in which pain-related words and social-threat words were paired with neutral (household) words. Stimulus pairs were presented for relatively brief (20ms) and relatively longer (1250ms) durations, which the authors argue tap into subliminal and supraliminal attentional biases, respectively (although these are typically referred to as 'voluntary' and 'involuntary' processes in the broader literature). Participants also completed self-report measures of abdominal pain symptoms (frequency and intensity) and body vigilance, whilst parents completed a measure of parent-reported anxiety and depression, and somatic complaints. Findings indicated that the youth with RAP demonstrated an attention bias *towards* subliminally-presented pain words, and *away* from supraliminally-presented pain words (in comparison to neutral words). The authors also found a trend for participants to attend to subliminal social threat words and to avoid supraliminal social-threat words (but $p < .10$ in both cases), and indeed repeated-measures analyses indicated that attention bias was not significantly different for pain and social-threat words. Age and sex were not significantly associated with attention bias scores. However, parent-reported child anxiety and depressive symptomatology was significantly positively associated with the child's attention bias towards supraliminally-presented pain words (but not subliminally-presented pain words). Interestingly, an attention bias towards (subliminally presented) social-threat words, but not pain words, was positively associated with participants' self-reported body vigilance and abdominal pain. Taken together, Boyer and colleagues (Boyer et al., 2006) provided the first evidence that youth with chronic pain show an attention bias towards pain-related versus neutral stimuli, with their findings particularly indicating a vigilance-avoidance pattern of attending. It is interesting, however, that this attention bias towards pain-related words did not significantly differ from a bias towards social-threat words, and that participants' self-reported levels of abdominal pain and body vigilance were associated only

with attending towards social-threat but not pain-related words, thus providing counterevidence for the content-specificity hypothesis described earlier.

A few years later, Beck and colleagues (J. E. Beck et al., 2011) performed a similar study, also with youth with FAP (N = 54, 10-16 years), and using the same dot-probe task. However, they also recruited a healthy control group (N = 53). Participants completed the dot-probe task before and after a laboratory stressor in which they were randomly assigned to be given failure or success feedback regarding their performance on a challenging computer game. Unlike Boyer and colleagues (Boyer et al., 2006), Beck and colleagues found that FAP patients exhibited selective attention *towards* supraliminally-presented pain words compared with neutral words, and compared with the control group, and this bias was maintained after negative feedback. For briefly-presented stimuli (20ms), FAP patients' bias was neutral at baseline, but increased significantly towards pain-related words after performance feedback both in the failure and success conditions. The authors thus argue that performance evaluation may activate FAP patients' involuntary attention bias to pain stimuli. Regarding social threat, neither the FAP patients nor control youth exhibited an attention bias toward social-threat stimuli at baseline, but both FAP and control youth significantly increased attention *away* from social-threat stimuli after failure feedback. Whilst it is interesting that FAP patients in this study did show an attention bias towards supraliminally-presented pain stimuli, their findings are in contrast to the earlier findings presented by Boyer and colleagues (Boyer et al., 2006), who found an attention bias away from these same stimuli. Thus, whilst both studies find some evidence that youth with chronic pain selectively process pain-related stimuli differently to neutral stimuli, there are conflicting findings in terms of direction of bias, making it difficult to draw firm conclusions.

More recently, van der Veek and colleagues (van der Veek et al., 2014) also administered a dot-probe task to youth with FAP and healthy controls, but employing more

personally-salient stimuli. Participants were shown sham pictures of their own bodily activity, in particular of their gut and heart activity. Electrocardiogram (ECG) stickers were placed on the participants' abdomen and on their chest to increase believability of the sham stimuli, and participants were shown images on a computer screen supposedly indicating the level of activity in those body parts. Participants also completed self-report measures of abdominal pain symptoms, anxious and depressive symptoms, other somatic complaints, and pain vigilance. Contrary to hypotheses, findings revealed no attentional bias for gut activity in either group. However, youth with FAP were slower than healthy controls on all supraliminal gut-activity trials, suggesting that pictures of gut activity may have distracted youth with FAP from the task they were performing (van der Veek et al., 2014).

Finally, Vervoort and colleagues (Vervoort, Trost, & Van Ryckeghem, 2013) have performed the only published study to date examining associations between attention bias and child experiences of experimentally-delivered pain. Fifty-nine youth (10-16 years) recruited from the community completed a dot-probe task with visual stimuli depicting pain-related and neutral facial expressions (500ms presentation time), before completing a CPT. Participants also completed a measure of pain catastrophizing, and Vervoort and colleagues (Vervoort, Trost, & Van Ryckeghem, 2013) considered the three subscales separately (rumination, helplessness, magnification). Findings indicated an attention bias away from pain faces relative to neutral faces among youth reporting greater pain magnification. In addition, youth who displayed an attention bias away from pain faces, and who reported greater pain magnification, also tolerated cold pressor pain for less time. Like in adult studies discussed above, degree of attention bias was not associated with experienced pain intensity.

Brief summary on cognitive bias and pain in youth

The study of pain-related cognitive biases in youth populations is clearly still in its infancy. There is preliminary evidence that youth with chronic pain, as well as healthy youth who have the tendency to magnify the negative consequences of pain, attend to pain-related information differently than neutral information. One study has also provided evidence that youth with chronic pain selectively attend to pain-related information differently than youth without chronic pain. However, the direction of pain-selective attention is unclear, particularly for stimuli presented for relatively longer durations (e.g., 500-1250ms). It is interesting that the study using the most personally-relevant stimuli (i.e., sham pictures indicating level of gut activity) did not find any evidence of selective attending for pain stimuli in youth with FAP compared to healthy controls. Nonetheless, taken together, the preliminary findings described above suggest that pain-related attention biases should continue to be investigated in youth populations.

On the basis of findings so far, as well as findings in adult pain populations and youth anxiety disorder populations, a number of questions could usefully be addressed in future studies. First, it is interesting that most studies in youth pain populations date (in fact, all studies with chronic pain samples) have recruited patients with abdominal pain. Although abdominal pain is the most common pain complaint in young people, it will be interesting to see if findings extend to patients with musculoskeletal pain, which characterise most adult populations in this field. Second, all published studies to date are cross-sectional, and thus give little indication as to the causal role of pain-related attention bias in youth. Whilst some studies have considered the role of attentional distraction in child acute pain experiences (e.g., (DeMore & Cohen, 2005; Kleiber & Harper, 1999), ABM studies will be useful to investigate the plasticity of attention biases in young people, and the impact of changing attention biases on pain outcomes, especially for youth with chronic pain. Finally, on the

basis that negative interpretation biases for ambiguous pain- and health-related information have been relatively consistently demonstrated in adults with chronic pain, it will be important to investigate the presence and role of interpretation bias in youth pain populations.

In addition to the points raised above, future research should consider the role of development in the emergence and impact of attention biases in youth pain populations. Indeed, despite growing evidence that pain-related cognitive biases are present in young people, and therefore develop before adulthood, studies to date have ignored the potential moderating role of developmental factors (Field & Lester, 2010). We can usefully draw from studies of cognitive bias in paediatric anxiety populations to identify developmental processes that may also play a role in the emergence and impact of cognitive biases in child and adolescent pain experiences.

1.4.2. Developmental considerations

One key question that has been identified in the study of paediatric anxiety is whether attention bias differentiates anxious from non-anxious children early in life, or whether associations between attention and anxiety change across child development. Whilst children as young as three years of age display symptoms associated with anxiety (Egger & Angold, 2006), the emotional Stroop and visual probe paradigms are too cognitively demanding for this age group (Field & Lester, 2010). Thus, researchers have used preferential looking paradigms to examine attention to threat in these samples. In comparison to work with older children, studies with young children have typically found an attention bias towards threat in all participants, regardless of anxiety levels or relevant precursors such as behavioural inhibition (see (Field & Lester, 2010) for a summary of findings). Data therefore appears to best fit a ‘moderation model’ of the development of attentional biases in paediatric anxiety (Field & Lester, 2010; Kindt & Van Den Hout, 2001; Salemink, van den Hout, & Kindt,

2007). That is, data suggests that child development moderates the expression of an existing attention bias, so that as children progress through development, some lose this bias, whilst for others (e.g., those with increased anxiety), the bias is maintained or heightened.

Kindt and colleagues suggest that the developmental mechanism driving this moderation is the protracted development of executive functioning, including attention control and cognitive inhibition, across childhood and adolescence. In particular, Kindt's Inhibition Hypothesis (Kindt, Bierman, & Brosschot, 1997; Kindt & Van Den Hout, 2001) proposes that whilst low anxious children develop the capacity to inhibit attentional biases towards threat, high anxious children are unable to do so. Although there has been very little empirical examination of this hypothesis to date (although see (Dudeney, Sharpe, & Hunt, 2015) for indirect evidence), a recent study by Susa and colleagues (Susa, Pitică, Benga, & Miclea, 2012) found that self-reported attention control, that is, the ability to shift and focus attention, significantly moderated the association between attention bias to threat and anxiety symptoms in a sample of youth. In particular, Susa and colleagues (Susa et al., 2012) found that the association between attention bias to threat and anxiety may be particularly strong when young people report low levels of attention control. These findings remain to be replicated, and it is yet unknown whether other executive functioning capacities (i.e., self-control and inhibition) have similar moderating roles. Nonetheless, there is preliminary evidence that child development, particularly in relation to executive functioning capacity, may be important for our understanding of attention bias in paediatric anxiety. The moderating role of executive functioning, including attention control, has also received interest in the study of cognitive biases in adult psychopathology populations. In particular, Dual Process Models (e.g., (Derryberry & Reed, 2002)) propose that psychopathology is a consequence of an imbalance between a fast, impulsive responding system, and a regulatory control system. Within this framework, attention control has been proposed as an important

variable moderating the association between attention bias to threat and adult anxiety disorders (Derryberry & Reed, 2002; Mathews & Mackintosh, 1998; Mathews & MacLeod, 2005). However, given the developmental importance of mastery over attention in adolescence (Cohen Kadosh, Heathcote, & Lau, 2014; Monk et al., 2003), and that there is protracted neuro-development of brain regions engaged in goal-directed attention during adolescence (Monk et al., 2003; C. A. Nelson et al., 2002; Spear, 2000a) the study of executive functioning as a moderator of the association between attention bias and anxiety may be particularly relevant in adolescent samples.

No studies to date have investigated the potential moderating role of attention control on the presence and impact of pain-related cognitive biases in child or adolescent populations. Given that findings on pain-related biases in youths are somewhat inconsistent (albeit there are few studies), examining processes such as attention control may generate an important step forward for our understanding in this emerging field. Indeed, it may be that an attention bias towards pain sensations and pain-related information is maladaptive only if the young person is unable to recruit effortful attention control to subsequently disengage their attention away from pain. On the other hand, given that a pattern of vigilance-avoidance for pain stimuli has been identified in youth with chronic pain (Boyer et al., 2006), and identified as a risk factor for pain chronicity in adult populations (Todd et al., 2015), it may instead be that effortful attention control is required to maintain attention on pain-related information to learn that it is not threatening, or to employ reappraisal strategies. Thus, on the basis of its potentially important role, attention control, particularly in moderating associations between attention biases and pain-related vulnerability factors, will be a central focus to the first three studies presented in this thesis.

1.5. Summary and Key Questions

The research presented in this introduction section makes a case for the importance of cognitive-affective processes, particularly for cognitive biases, in chronic pain disorders. Manipulating attention and interpretation biases may have a causal influence on pain experiences, but research in this area is still in its infancy. The presence and role of pain-related cognitive biases in adults is now well investigated, at least for attention biases. There are far fewer published studies with youth samples, although preliminary findings suggest that selective attending towards and away from pain may also be associated with chronic pain in youth. To date, there are no studies investigating biased interpretations of ambiguous information, although studies do indicate that appraisal processes (particularly pain catastrophizing) play an important role in young people's pain experiences.

The primary aim of this thesis is to investigate the role and plasticity of pain-related cognitive biases in adolescents. The studies presented in this thesis address three key questions:

Research Question 1) Is an attention bias towards pain-related information associated with pain-related vulnerability factors in adolescence, and does attention control moderate this association?

Research Question 2) Is an attention bias towards pain-related information malleable to change, and can these changes impact pain-related outcomes in adolescents with chronic pain?

Research Question 3) Is a negative interpretation bias for pain-related and bodily-threat information associated with pain-related vulnerability factors, and chronic pain, in adolescence?

These issues will be addressed in the following experimental chapters:

Chapter Two will address Research Question One. In particular, it investigates associations between pain catastrophizing and attention bias towards pain-related stimuli in a community sample of adolescents, and examines whether attention control moderates associations. Attention bias is measured using a dot-probe task presenting images of adult pain and neutral facial expressions for relatively short (100ms) and longer (1250ms) durations, to index relatively early and later stages of attentional processing. Pain catastrophizing is measured using a self-report questionnaire asking participants to report on how much they normally catastrophize when in pain (the Pain Catastrophizing Scale – Child version (PCS-C); (Crombez et al., 2003)). Attention control is also indexed by a self-report questionnaire, asking participants to report how well they are able to control their attention in everyday life (the Attention Control Scale (ACS); (Derryberry & Reed, 2002)).

Chapter Three will also address Research Question One, and is designed to build on findings from Chapter Two by employing a stronger methodological design. Attention bias is measured using eye-tracking during a free viewing task in which participants view photographs of young people displaying pain (and neutral) facial expressions. Images are presented for 3000ms, and indices of initial fixation and fixation duration are calculated to index relatively early and later stages of attention. Particularly important, participants are informed that the photographs were taken whilst the pictured children completed the cold pressor test (CPT), a task that they will also subsequently complete. Thus, stimuli are personally relevant for an upcoming pain experience. In addition, state levels of catastrophizing and anxiety in the face of completing the CPT are measured. As in Chapter Two, attention control is measured with the self-report ACS (Derryberry & Reed, 2002).

Chapter Four will address Research Question Two. In particular, it investigates the plasticity of pain-related attention biases in adolescents with chronic pain, and the impact of

Attention Bias Modification (ABM) on pain symptomatology, pain catastrophizing, anxiety and depression symptoms, and disability. Adolescents with chronic pain are randomly assigned to complete eight bi-weekly sessions of dot-probe ABM or placebo training, or to a waitlist control group. As above, pain catastrophizing is measured using the PCS-C (Crombez et al., 2003). Generalised anxiety and depression symptoms are measured using the self-report Revised Children's Anxiety and Depression Scale (RCADS; (Chorpita, Yim, Moffitt, Umemoto, & Francis, 2000)). Disability is measured using the self-report Functional Disability Inventory (FDI; (Walker & Greene, 1991)) as well as two physical tasks (the sit-to-stand task and the cardio wall task). Given the findings presented in earlier chapters, we also investigate the impact of ABM on attention control. Attention control is indexed using a self-report measure (the ACS; (Derryberry & Reed, 2002)) as well as an experimental measure (the Fish Flanker; (Rueda et al., 2004)).

Chapter Five will address Research Question Three. In particular, it considers the role of interpretation bias in adolescent pain experiences. We first develop and pilot a novel measure of pain-related interpretation bias in a large community sample of adolescents; the Adolescent Interpretations of Bodily Threat (AIBT) task. The AIBT task presents ambiguous bodily-threat as well as ambiguous social situations. Using this task in a separate community sample of adolescents, we then investigate associations between a negative interpretation bias and pain catastrophizing as well as recent pain experiences. As in previous chapters, pain catastrophizing is measured using the PCS-C (Crombez et al., 2003). Participants also complete the RCADS (Chorpita et al., 2000) to index anxiety and depression symptoms. Finally, participants rate their average pain intensity and worst pain intensity in the past three months (0 = no pain; 10 = worst pain possible), the amount that pain has interfered with daily activities over the past three months (0 = I don't miss out on any activities; 10 = I miss out on all activities), and the frequency of their pain over the past three months (1 = on less than 1

day each month; 6 = every day) (items taken from the Brief Pain Inventory (BPI); (Cleeland & Ryan, 1994)), to index recent pain experiences.

Chapter Six will also address Research Question Three, and was designed to build on findings from Chapter Five by administering the AIBT task to adolescents with chronic pain (n.b. these were the same participants as in Chapter Four). Adolescents with chronic pain are compared to participants from Chapter Five who reported no pain problems. Adolescents with chronic pain also complete the FDI (Walker & Greene, 1991), BPI (Cleeland & Ryan, 1994), and RCADS (Chorpita et al., 2000) to index functional disability, severity of chronic pain, and anxiety and depression symptoms, respectively.

Chapter 2

An edited version of this chapter has been published as follows:

Heathcote, L. C., Vervoort, T., Eccleston, C., Fox, E., Jacobs, K., Van Ryckeghem, D. M., & Lau, J. Y. (2015). The relationship between adolescents' pain catastrophizing and attention bias to pain faces is moderated by attention control. *Pain, 156*(7), 1334-1341.

2

The Relationship between Adolescents' Pain Catastrophizing and Attention Bias to Pain Faces is Moderated by Attention Control

This study considered the attentional functioning of adolescents with varying levels of pain catastrophizing. Specifically, we investigated the relationship between pain catastrophizing and attention bias to pain facial expressions. Further, drawing on dual process models in the context of pain, we investigated the moderating role of attention control on this relationship. Adolescents (*N*=73, 16-18 years) performed a dot-probe task in which facial expressions of pain, and neutral expressions, were presented for 100ms and 1250ms. Participants also completed self-report pain catastrophizing and attention control measures. We found that while there was no main effect of pain catastrophizing on attention bias towards pain faces, attention control did significantly moderate this relationship. Further analysis revealed that lower levels of attention control were significantly associated with increasing attentional vigilance towards pain faces only within high catastrophizing adolescents. In addition, we found that poorer attention control was related to increased attention bias for pain faces (regardless of pain catastrophizing level) when these faces were presented for relatively longer durations, but not for shorter durations. This study supports a dual process model of attentional processes in pain, thus replicating previous findings within the psychopathology literature but extending them to the study of pain.

2.1. INTRODUCTION

Pain functions to capture attention, motivating avoidance of potential bodily harm (Eccleston & Crombez, 1999). However, when pain is perceived as potentially severe or harmful, individuals may selectively attend to pain and cues for pain over competing demands. Consequently, these individuals may experience increased attentional capture and disruption by pain. This may be particularly true among individuals who catastrophize about pain, characterized by excessive magnification and elaboration regarding the causes and consequences of pain (Wilson & MacLeod, 2003). Indeed, some findings have indicated that attentional capture by pain/pain-related information (termed Attention Bias) is amplified with greater pain-related catastrophizing (Caes, Vervoort, Eccleston, Vandenhende, & Goubert, 2011; Crombez, Eccleston, Baeyens, & Eelen, 1998; Heyneman, Fremouw, Gano, Kirkland, & Heiden, 1990; Karsdorp, Ranson, Schrooten, & Vlaeyen, 2012; Michael J L Sullivan et al., 2001; Michael J. L. Sullivan, Bishop, & Pivik, 1995; Van Damme, Crombez, & Eccleston, 2004). However, evidence is not unequivocal; some studies fail to identify expected relationships (Crombez et al., 2013; Huber, Kunz, Artelt, & Lautenbacher, 2010; Roelofs, Peters, van der Zijden, Thielen, & Vlaeyen, 2003; Van Ryckeghem et al., 2013; Verhoeven et al., 2010), and others find evidence counter to expectations (Boston & Sharpe, 2005; Vervoort, Caes, Trost, Notebaert, & Goubert, 2012; Vervoort et al., 2006). These findings suggest that the relationship between attention bias to pain and pain catastrophizing may be moderated by other variables.

Attention control, the ability to focus effortfully in the face of distraction and flexibly shift attention, is likely to be important in understanding the variable relationship between pain catastrophizing and attention bias to pain. This suggestion draws on dual process models - mostly invoked in the context of anxiety disorders (Derryberry & Reed, 2002) - in which anxiety is a consequence of an imbalance between a fast, impulsive responding system, and a

regulatory control system. Specifically, attention control has been proposed as an important variable moderating the association between anxiety and attention bias to threat (Derryberry & Reed, 2002; Mathews & Mackintosh, 1998; Mathews & MacLeod, 2005; Susa et al., 2012). Studies have indeed revealed that only anxious participants with poor attention control show an attention bias towards threat (Derryberry & Reed, 2002; Susa et al., 2012). Recently, these findings were extended to a sample of chronic fatigue patients (Hou et al., 2014). However, no studies have investigated such dual process models within the context of pain. Furthermore, there are no studies with younger people, despite the developmental importance of mastery over attention in adolescence (Cohen Kadosh et al., 2014; Monk et al., 2003), and the neuro-development of brain regions engaged in goal-directed attention (Monk et al., 2003; C. A. Nelson et al., 2002; Spear, 2000b). Indeed, only one published study to date has investigated the relationship between pain catastrophizing and attention bias to pain in a sample of youth, but without considering attention control (Vervoort, Trost, & Van Ryckeghem, 2013).

Our interest is in the attentional functioning of adolescents with varying levels of pain catastrophizing. We had two objectives. First, to examine the relationship between adolescent pain catastrophizing and attention bias to visual pain stimuli (facial expressions), assessed using dot-probe methodology. Second, to examine the moderating role of adolescents' self-reported attention control on the relationship between pain catastrophizing and attention bias. Based on predictions of the dual process model, we hypothesized that (1) adolescents' level of pain catastrophizing would be positively associated with an attention bias towards pain faces, and (2) self-reported attention control would further moderate the association between pain catastrophizing and attention bias to pain faces such that catastrophizing would relate to attention bias particularly when attention control is low. Additionally, because attention is

temporal and dynamic, we presented pain faces at two presentation times, to explore the hypothesized associations at early and later stages of processing.

2.2. METHODS

Participants

Participants were recruited from two educational establishments (a senior school and a further education college) in the south of England. Research assistants contacted both educational establishments, and the principals gave verbal consent to make contact with adolescents as potential participants. All participants were completing A-level qualifications (Year 12 or senior year). A teacher at the school contacted all participants, inviting them to take part in the study during regular school hours. We conducted a brief screening with teachers to exclude participants who were suffering from chronic pain. No participants were identified and thus excluded. Participants gave written informed consent. We invited eight school classes to take part, 78 adolescents, who all agreed to participate. Exclusion criteria included visual difficulties or a learning disability. Two participants were excluded from analysis on the basis that they did not complete at least 25% of items on one or both of the questionnaires. Due to technical issues in retrieving recorded dot-probe data, two additional participants were excluded. One participant was excluded from analysis as he had turned 19 by the testing session date.

The final sample entered in the analyses consisted of 73 adolescents (56 girls) aged 16-18 years (M = 16.8 years, SD = 0.72). The study was approved by the University of Oxford Central University Research Ethics Committee.

Measures

Adolescents' catastrophic thinking about pain was assessed with the Pain

Catastrophizing Scale for Children (PCS-C) (Crombez et al., 2003). This instrument is adapted from the adult Pain Catastrophizing Scale (Michael J. L. Sullivan et al., 1995). The PCS-C also consists of 13 items, and yields a total score that can range from 0 to 52, with higher scores indicating more pain catastrophizing, as well as three subscale scores for rumination (e.g., *"when I am in pain, I keep thinking of other painful events"*), magnification (e.g., *"when I am in pain, I become afraid that the pain will get worse"*), and helplessness (e.g., *"when I am in pain, I feel like I can't go on like this much longer"*). The PCS-C has been shown to be both reliable and valid for children above 9 years (Crombez et al., 2003). Cronbach's alpha in this study was .93 for the total score.

Adolescents' attention control was assessed with the Attention Control Scale (ACS) (Derryberry & Reed, 2002). The ACS consists of 20 items, and yields a total score that can range from 20 to 80, with higher scores indicating good attention control. The ACS has two subscale scores for attention focusing (e.g., *''my concentration is good even if there is music in the room around me''*) and attention shifting (e.g., *"It is easy for me to alternate between two different tasks"*). The ACS has shown good reliability and predictive utility, predicting resistance to interference in Stroop-like spatial conflict tasks as well as attentional disengagement from threat stimuli among highly anxious people (Derryberry & Reed, 2002). Furthermore, Matthews and colleagues (Mathews, Yiend, & Lawrence, 2004) showed greater activation in brain areas related to top-down regulation of emotion (i.e., rACC) in those reporting greater attention control. Attention control has also been measured with good reliability and validity in children (Muris, de Jong, & Engelen, 2004). Cronbach's alpha in this study was .83 for the total score.

Stimulus Materials

The stimulus set consisted of 12 pictures of 6 adult faces (3 male and 3 female). All pictures were drawn from one-second video clips of simulated facial expressions of pain. These pictures were taken from a larger collection of stimuli, previously created and validated in the laboratory by Simon and colleagues (Simon, Craig, Gosselin, Belin, & Rainville, 2008), who provided permission for using these stimuli. For these stimuli actors were videotaped while producing neutral facial displays and simulated facial expressions of different pain intensities. For this study, we used neutral facial expressions and facial expressions of moderate pain. We selected facial expressions of moderate rather than severe pain on the basis of evidence that differences in *anxiety*-linked vulnerability may reflect the intensity of stimulus threat required to elicit the attentional vigilance response. That is, whilst strongly threatening stimuli have been shown to universally attract attention as an adaptive mechanism, moderately threatening stimuli may be more sensitive to picking up anxiety-linked differences in attentional responding (see (Mathews & Mackintosh, 1998; Karin Mogg & Bradley, 1998)). We expected similar findings for pain-related differences in attentional responding, that is, more ambiguous facial expressions would reveal greater variability among individuals. Using these 12 pictures, six study slides were generated. Each slide consisted of two pictures of the same adult, presenting a neutral face or a moderate pain face. Using the Facial Action Coding System (Ekman, Friesen, & Hager, 2002), these video clips were previously reliably coded on occurrence and intensity of facial expression of pain (Simon et al., 2008). Furthermore, two neutral pictures of two other adult faces from the Simon stimulus set were selected to create filler trials which consisted of a neutral-neutral picture pair of the same adult face. Additionally, two pictures of two other neutral faces used previously by Vervoort and colleagues (Vervoort, Trost, & Van Ryckeghem, 2013) were selected for the practice trials. The present stimuli have been used in prior research

examining attention bias to pain (see (Vervoort et al., 2012)). The validity of the present stimulus set used during the experimental phase is supported by previous findings of significantly different observer pain ratings between neutral and moderate pain facial expressions (see (Vervoort, Trost, & Van Ryckeghem, 2013)).

Dot-Probe Task

The dot-probe task measures attention bias by simultaneously presenting a pain-related and neutral stimulus, one of which is then replaced by a shape (in this case, a white rectangle). Participants are required to make a decision about the location of the rectangle, and whilst pain-related and neutral stimuli are not critical for responding, attention capture is inferred by speeded reaction times to the rectangle in a location where a pain-related or neutral stimulus was previously presented.

All stimuli were presented against a black background. Each trial began with a 500ms presentation of a white fixation cross in the middle of the screen. Participants were instructed to fixate their gaze on this location. Then, one picture pair appeared and remained visible for either 100ms (50% of the trials) or 1250ms. Each facial image in this pair was 47mm in width and 78mm in height. One of the pictures was presented above and one below the fixation cross, with the centre of the pictures positioned 57mm above and below (respectively) the centre of the screen. Immediately after the offset of these two pictures, a small white rectangle (0.9/1mm; the probe) was presented at the location of one of the pictures. Participants had to indicate the probe location by pressing one of two buttons as quickly and accurately as possible on a QWERTY keyboard. The 'q' key was pressed with the left index finger when the probe was presented at the upper location, and the 'm' key was pressed with the right index finger when the probe was presented at the lower location. Stickers showing up and down arrows were placed on the 'q' and 'm' keys respectively to

help participants with responding. A new trial started after a response, or automatically when 2500ms elapsed without response. When a participant responded erroneously, the term 'error' briefly appeared on the screen (200ms). To reduce possible habituation to pain-related stimuli that might occur if all trials contained pain-related information, filler trials (neutral picture pairs presented for 100ms (50%) or 1250ms) were included. Further, in order to ensure that participants maintained gaze at the middle of the screen, a number of digit trials were presented (see e.g., (Van Ryckeghem, Crombez, Van Hulle, & Van Damme, 2012)). In these trials, the fixation cross was followed by a randomly selected digit between one and nine for a duration of 100ms. Participants were instructed to type the number on the keyboard. Pictures were presented in randomized order across trials and participants. Trials were intermixed and randomly presented in two blocks, with a break between block one and block two. For each participant, the target pictures as well as the probe were presented equally often at the top or bottom position of the screen in four possible combinations: target top/probe top; target top/probe bottom; target bottom/probe bottom; target bottom/probe top. Thus, the probe was equally likely to replace either a pain face or neutral face. In the context of the current study, *congruent* trials were those where the probe was presented at the same location as the pain face. *Incongruent* trials were those where the probe was presented at the same location as the neutral face. Each picture pair was presented 32 times. The inter-trial interval was 200ms after picture trials, or 1100ms after digit trials to allow participants to place their fingers back on the 'q' and 'm' buttons. The task began with 16 practice trials consisting of neutral face-pairs, none of which appeared in the experimental trials. The test phase consisted of 192 test trials, 64 filler trials, and 18 digit trials. The dot-probe task was programmed and presented using the INQUISIT Millisecond software package. INQUISIT measures response times (RTs) with millisecond accuracy (Inquisit 4.0; Millisecond Software, Seattle, WA, USA).

Split half reliability calculations indicated low internal consistency; Spearman-Brown Coefficients were -.28 and .27 for attention bias indices at 100ms and 1250ms, respectively.

Procedure

Upon arrival, participants were allocated participant numbers and then completed the informed consent form. Participants were informed that they would first complete a computer task, and afterwards would be asked to fill out questionnaires using an online format. Participants were seated in front of a computer at a distance of approximately 60cm from the screen. Instructions for the dot-probe task were presented on the computer screen. Participants were informed that they would see several pictures of individuals undergoing a painful procedure. The experimenter watched the participant whilst s/he performed practice trials to ensure that s/he understood the instructions. Participants were given the following instructions: "During this computer task, a white cross will be shown at the centre of the screen. Try to focus your eyes on this cross when it appears. After the white cross appears, two pictures of people will be shown. One picture will be shown at the top of the screen, one picture will be shown at the bottom of the screen. Immediately after the pictures are shown, a small white rectangle will appear in place of one of the pictures (i.e., at the top or bottom part of the screen). Your task is to indicate, using two keys on the keyboard, as fast as possible, where you have seen the rectangle. Press 'q' when you have seen the rectangle at the upper part of the screen. Press 'm' when you have seen the rectangle at the bottom part of the screen. Try to be as fast and accurate as possible. Sometimes, a number will be shown at the location of the white cross. When this happens, you have to type this number using the keyboard. Try to make as few errors as possible." Participants were also informed that there would be a break in the middle of the computer task, and that they should take around one minute to silently look away from the computer screen. After completing the dot-probe task,

participants completed the questionnaires. Upon completion, participants were debriefed as to the nature of the study, and given a £5 Amazon voucher.

Data reduction and statistical plan

To investigate *the relationship between adolescent pain catastrophizing and selective attention to pain* (i.e., hypothesis 1), mean response times (RTs) on congruent and incongruent trials were used as dependent variables in the analyses. Analyses employed a 2 × 2 factorial repeated measures design with congruency (congruent / incongruent) and presentation time (100ms / 1250ms) as within subject factors and adolescent centred pain catastrophizing score entered as a covariate. Repeated measures ANOVA was chosen since the design of our study include presentation time as a within-subjects variable and we were interested in whether the effects of pain catastrophizing and selective attention to pain varied across presentation times. Pain catastrophizing was entered as a covariate in order to retain the full range of scores on this continuous measure, rather than arbitrarily splitting participants into groups, thereby retaining greater variance to observe relationships. In case of a significant catastrophizing x congruency interaction, attention bias indices were calculated to ease interpretation of the direction of differences between congruent and incongruent trials, and Pearson correlation analyses were performed to examine their relationship with catastrophizing. Bias scores were calculated by subtracting the average response time on congruent trials from the average response time on incongruent trials. A positive bias index indicates increased selective attention to pain faces, whereas a negative index is indicative of attentional avoidance. A mean bias index (across 100ms and 1250ms) was calculated in case the congruency x catastrophizing x presentation time three-way interaction did not reach significance, whereas separate bias indices were calculated for 100ms and 1250ms and used within separate analyses in case the three-way interaction also reached significance.

For all analyses, the cut-off for statistical significance was set at $p < .05$, and effect sizes were reported using the Partial Eta Squared index (ηp^2). Following Cohen (Cohen, 1988) and Olejnik and Algina (Olejnik & Algina, 2000); small effect size = 0.01; medium effect size = 0.06; large effect size = 0.14.

To investigate *the potential moderating role of attention control on the relationship between adolescent pain catastrophizing and selective attention to pain* (i.e., hypothesis 2), analyses were re-run but with the centred attention control score also entered as a covariate. Again a repeated measures ANOVA was selected in order to reflect the within-subject variable of presentation time, which could moderate the effects of our key variables. In case of a significant catastrophizing x congruency x attention control three-way interaction, additional moderation analyses were performed to interpret interaction effects (i.e., whether the association between the predictor variable (pain catastrophizing) and the outcome variable (attention bias) is significant only for high levels of the moderator variable (attention control), low levels of the moderator variable, or both). Moderation analyses followed the procedure outlined by Holmbeck (Holmbeck, 2002). To this end, two steps were performed. First, two new conditional continuous moderator variables were computed by (1) subtracting one SD from the centred moderator variable (high levels of adolescent attention control) and (2) adding one SD to the centred moderator variable (low levels of adolescent attention control). Next, two additional ANCOVAs were performed - incorporating each of these new conditional continuous moderator variables - to test the significance for low (1 SD below the mean) and high (1 SD above the mean) values of the conditional moderator variable. In case of significant three-way interactions including presentation time, congruency, and one of the continuous variables (ie., either attention control or pain catastrophizing), we calculated separate correlation analyses between the continuous variables and the attention bias indices (i.e., attention bias at 100ms and attention bias at 1250ms) to ease interpretation of direction

of effects (see (Koster, Crombez, Verschuere, & De Houwer, 2004) for similar procedure). In case the four-way interaction (i.e., including presentation time) also reached significance, these analyses were performed separately for 100ms and 1250ms, otherwise the average bias index (across 100ms and 1250ms) was used. In all analyses, Greenhouse-Geisser corrections (with adjusted degrees of freedom, or NDf) were performed whenever the sphericity assumption was violated (Mauchly's test of sphericity was $p < .05$).

2.3. RESULTS

Participant characteristics

The mean level of adolescents' pain catastrophizing was 21.62 (*SD* = 11.03), and the mean level of attention control was 47.15 (*SD* = 8.51). Girls reported significantly higher levels of pain catastrophizing compared to boys ($t(71) = -2.01$, $p < .05$, $d = .48$), but did not differ on the measure of attention control ($t(71) = 1.49$, ns, $d = .35$). Pain catastrophizing was significantly negatively correlated with attention control ($r = -.26$, $p < .05$). No significant correlations were observed with child age (both $r \leq .21$, ns).

Attention bias analyses

Data preparation

Consistent with previous research (Van Ryckeghem et al., 2012), trials with errors and responses shorter than 200ms or longer than 2000ms were discarded. Within the present sample, the number of errors made by participants ranged from 0 to 24 (*M* = 5.73), and .05% of the RTs fell outside the 200ms – 2000ms range. Probe detection latencies that were three standard deviations above or below the individual mean RT of corrected responses were also considered outliers and excluded from analyses (see (Koster et al., 2004)). This was the case for 1.43% of the RTs. Thus, statistical analyses were run on 96.34% of the data.

The relationship between adolescent pain catastrophizing and selective attention to pain

Mean RTs and SDs on different trial types are presented in Table 2.1. The RTs were analysed using a 2 (congruency: congruent / incongruent) x 2 (presentation time: 100ms / 1250ms) repeated measures ANCOVA with pain catastrophizing entered as a covariate. Analyses revealed no main effect of congruency ($F(1,71) = .27$, ns, $\eta p^2 = .004$), indicating no overall selective attention to pain. Likewise, there was also no significant effect of catastrophizing ($F(1,71) = .50$, ns, $\eta p^2 = .007$) or presentation time ($F(1,71) = 2.88$, ns, $\eta p^2 = .039$), nor were there any significant two or three way interactions (all $F \leq .88$, ns, all $\eta p^2 \leq .012$), indicating that attention deployment to either pain or neutral faces did not depend upon adolescents' level of pain catastrophizing, presentation time (i.e., 100ms / 1250ms), or the interaction between both.

Table 2.1: *Mean reaction times (in milliseconds) and standard deviations (SD) on congruent and incongruent trials for 100ms and 1250ms presentation time*

Presentation time	Congruent trials	Incongruent trials
100ms	454 (55)	453 (53)
1250ms	458 (53)	459 (56)

The moderating role of attention control in the relationship between adolescent pain catastrophizing and selective attention to pain

To investigate the moderating role of attention control, a similar repeated measures ANCOVA was run but with the centred attention control score also entered as a covariate. Analyses revealed a significant three-way interaction of pain catastrophizing with congruency and attention control ($F(1,69) = 4.55$, $p < .05$, $\eta p^2 = .062$), indicating that the relationship between pain catastrophizing and attention bias to pain is dependent upon levels of attention

control. Furthermore, there was also a significant attention control x congruency x presentation time interaction ($F(1,69) = 4.26$, $p < .05$, $\eta p^2 = .058$), indicating that the relationship between attention control and attention bias to pain varies with different presentation times (10ms / 1250ms). No other main or interaction effects were observed (all $F \leq 3.75$, ns, all $\eta p^2 \leq .051$). Below, we first report on the three-way interaction between pain catastrophizing, congruency, and attention control, and we then report on the three-way interaction between attention control, congruency, and presentation time.

To interpret the significant pain catastrophizing x congruency x attention control interaction, two univariate ANOVAs were performed with the average bias index (i.e., across 100ms and 1250ms) entered as the dependent variable, pain catastrophizing as the predictor variable, and high (1SD above the mean) or low (1SD below the mean) values of self-reported attention control as a covariate. As shown in Figure 2.1, findings indicated a cross-over interaction, indicating that pain catastrophizing differentially impacted attention bias to pain dependent upon high vs. low levels of adolescents' attention control. Specifically, for adolescents reporting *high* levels of attention control, pain catastrophizing was negatively associated with attention to pain. Conversely, for adolescents reporting *low* levels of attention control, pain catastrophizing was positively associated with attention to pain. While these patterns did not significantly differ from zero for adolescents reporting low attention control ($F(1,69) = 1.13$, ns, $\eta p^2 = .016$) and only approached significance for adolescents reporting high attention control ($F(1,69) = 3.31$, $p = .07$, $\eta p^2 = .046$), the significant cross-over interaction indicates these patterns are significantly different from each other. Inspection of Figure 2.1 also suggests that attention control affects attention bias to pain differently for high catastrophizing adolescents relative to low catastrophizing adolescents. Indeed, additional analyses *within high catastrophizing* adolescents showed that attention control was negatively associated with attention bias to pain such that lower levels of attention control

were associated with increasing attention bias towards pain ($F(1,69) = 5.96$, $p < .05$, $\eta p^2 = .08$). Attention control was not associated with attention bias to pain for low catastrophizing adolescents ($F(1,69) = .52$, ns, $\eta p^2 = .007$). Re-running analyses whilst also controlling for adolescent gender revealed similar main effects and interactions between pain catastrophizing x congruency x attention control, and attention control x congruency x presentation time, with no additional significant terms involving gender.

To interpret the significant attention control x congruency x presentation time interaction, which indicates that the relationship between attention control and attention bias to pain varies with different presentation times, separate Pearson correlation coefficients were calculated between adolescents' attention control score and the attention bias index at 100ms and 1250ms, respectively. Findings indicated attention control was significantly negatively correlated with the attention bias index at 1250ms ($r = -.24$, $p < .05$). No significant correlation was observed for the attention bias index at 100ms ($r = .05$, ns).

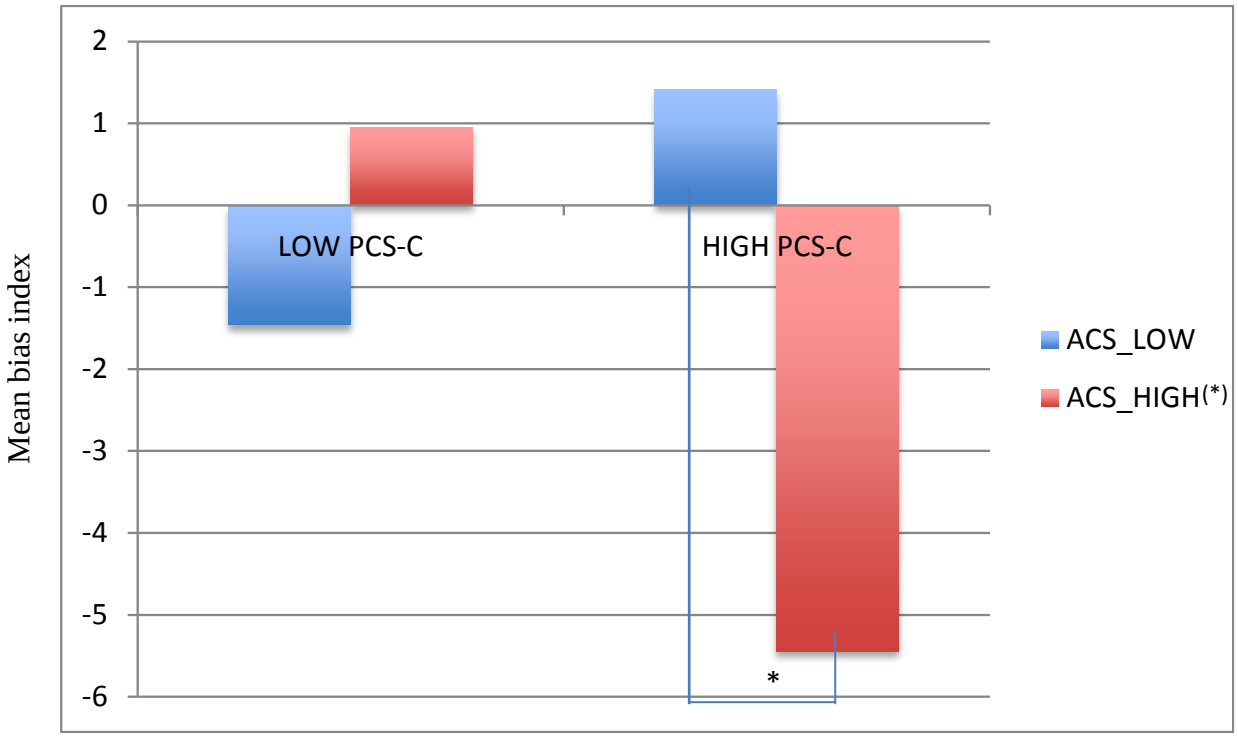


Figure 2.1: Average bias indices for pain faces as a function of low (1SD below the mean) and high (1SD above the mean) levels of adolescents' attention control *$p < .05$; (*)$p < .10$

2.4. DISCUSSION

In this study, we investigated the relationship between pain catastrophizing and attention bias to facial expressions of pain in adolescents. We further investigated the moderating role of self-reported attention control. We hypothesized that (1) adolescents' level of pain catastrophizing would be associated positively with an attention bias towards pain faces, and (2) attention control would moderate the association between pain catastrophizing and attention bias to pain faces. Results partially supported our hypotheses. While there was no main effect of pain catastrophizing on attention bias towards pain, attention control did significantly moderate this relationship. We found a cross-over interaction indicating that whereas pain catastrophizing was negatively associated with attention bias to pain among adolescents reporting high attention control, the opposite pattern was observed among adolescents reporting low attention control. While separate analyses examining effects at low and high attention control did not reach significance, the observed cross-over interaction suggests that low levels of attention control are relevant in understanding increasing attention to pain stimuli among high pain catastrophizing adolescents. Indeed, lower levels of attention control were significantly associated with increasing vigilance towards pain faces only within high catastrophizing adolescents. No such pattern emerged among low catastrophizing adolescents. We also found that poorer attention control was related to increased attention bias for pain faces (regardless of pain catastrophizing level) when these faces were presented for relatively longer durations but not for short durations.

To our knowledge, this is the first study to examine the relationship between attention bias toward pain-related information, level of attentional control, and individual differences in catastrophic beliefs about pain and its consequences. The study was cast within and supports a dual process model of attentional processes in pain. Dual process models provide a theoretical account of how phenomena occur from both implicit and explicit processes, and

have furthered our understanding of several clinical disorders. For example, adult (Bardeen & Orcutt, 2011; Derryberry & Reed, 2002; Hou et al., 2014; Schoorl, Putman, Van Der Werff, & Van Der Does, 2014) and paediatric (Helzer, Connor-Smith, & Reed, 2009; Susa et al., 2012) studies have demonstrated that attention control moderates the relationship between *anxiety-related* variables (e.g., trait and state anxiety, post-traumatic stress symptoms) and attention bias to threat. Our study extends these previous findings within the psychopathology literature to the study of pain. We find that both automatic and controlled attentional processes are important in the relationship between attention to pain and pain cognitions. As such, these findings may explain why some studies find positive associations between pain catastrophizing and attention bias (Karsdorp et al., 2012; Van Damme et al., 2004; Vervoort et al., 2012), whilst others find negative or no associations (Boston & Sharpe, 2005; Vervoort et al., 2012, 2006). Our findings may have implications for the literature on Attention Bias Modification (ABM), a training technique that targets and shifts attention biases, possibly by enhancing attention control. These ABM techniques have been employed mostly to reduce anxiety and depression, but are being extended to adult pain conditions (M. Dehghani, Sharpe, & Nicholas, 2004; Sharpe et al., 2012, 2015). Although not definitive, there is some suggestive data that ABM may increase attention control, rather than shift biases per se (Browning, Holmes, & Harmer, 2010). Our findings indeed suggest that attention control may be important to the association between pain catastrophizing and attention bias, perhaps allowing individuals to subsequently disengage from pain-related threat.

This study also extends the limited paediatric literature examining attention biases within the context of pain, with only four published studies (J. E. Beck et al., 2011; Boyer et al., 2006; van der Veek et al., 2014; Vervoort, Eccleston, Goubert, Buysse, & Crombez, 2010), and among these, only one within the context of pain catastrophizing (Vervoort et al., 2010). This dearth of research is surprising given the significant number of children suffering

from (chronic) pain (King et al., 2011), the hypothesized pivotal role of attention in the development and maintenance of pain problems (Asmundson et al., 2012), the importance of pain catastrophizing in understanding deleterious pain outcomes (e.g., increased pain/disability) among clinical and nonclinical paediatric samples (Crombez et al., 2003), and the need for novel treatment approaches targeting anxiety-related factors in paediatric chronic pain patients (Fisher et al., 2014). Furthermore, given neuroimaging and behavioural evidence (Blakemore & Choudhury, 2006; Cohen Kadosh et al., 2014; Monk et al., 2003) that brain areas underlying executive functions such as attention control are still developing during adolescence, examining attention control as a moderating factor on the association between pain catastrophizing and attention bias to pain-related stimuli may be particularly important within adolescence. Samples spanning childhood, adolescence, and adulthood will be important to examine whether and at what point in child development these associations are most stable.

The present study is also one of few studies to explore attentional capture by pain temporally (at 100ms and 1250ms stimulus presentation times; see also (Baum et al., 2013)), and is the first study to do so with adolescents. We found an additional interaction between attention control, congruency, and presentation time, suggesting that the relationship between attention control and attention bias to pain faces varies at early and later stages of processing. Specifically, adolescents high in attention control selectively avoided pain faces at the longer but not shorter presentation time. This is perhaps unsurprising, given the inherently aversive nature of pain facial expressions, and the fact that 1250ms (but not 100ms) is arguably enough time to exert effortful attentional control to shift away from aversive stimuli. Importantly, while our results may at first seem different to a recent meta-analysis revealing a more pronounced attention bias *towards* pain-related information when stimuli were presented for 1250ms (Schoth et al., 2012), this is not necessarily the case, as the studies

included in the meta-analysis did not consider whether associations varied with attention control. Furthermore, the current study comprised healthy adolescents, whereas the meta-analysis included only adults with chronic pain, limiting the generalizability of the meta-analysis findings. Interestingly, we found no effect of presentation time on the association between pain catastrophizing and attention control in predicting attention bias (as indicated by a non-significant four-way interaction), suggesting that attention control moderates the association between pain catastrophizing and both early and later attentional capture by pain stimuli in a similar way. Future studies should replicate our findings and examine the efficacy of briefly presented stimuli to capture attention in youth. Future studies may also benefit from using technologies such as eye-tracking (see e.g., (Vervoort, Trost, Prkachin, & Mueller, 2013)) to further reveal the temporal nature of this relationship. Eye-tracking technologies could supplement dot-probe methodology used in this study by providing continuous indices of the focal point of attention, allowing precise examination of the temporal dynamics of selective attention in youth, and by overcoming issues of reliability reported in the present study and in previous studies (Dear, Sharpe, Nicholas, & Refshauge, 2011b).

This study has limitations. First, most of our sample is female. Second, we used an unselected adolescent sample, and did not collect detailed information regarding pain history. We relied on a brief screening with teachers to exclude participants who were suffering from chronic pain. Nonetheless, given epidemiological findings, we might expect that some individuals in our sample were experiencing recurrent pain, which could have impacted our findings. Third, we used painful faces as salient threat cues. Facial stimuli limit us to investigating general effects that are not specific to individual participants. Future studies may benefit by increasing personal salience of stimuli, such that pain faces cue a potential personal pain experience (see e.g., (Vervoort, Trost, & Van Ryckeghem, 2013)). Fourth, we used a single, self-report measure of attention control. Whilst the ACS has shown good utility

in predicting attentional performance in experimental tasks (Derryberry & Reed, 2002), it will be important for future studies to also include other measures of attention control such as flanker tasks (that are reliant on behavioural responses and reaction times) as well as antisaccade tasks (that are reliant on eye movement patterns) (e.g., (Eriksen & Eriksen, 1974; Fan, McCandliss, Sommer, Raz, & Posner, 2002; Hutton & Ettinger, 2006)). These measures may be particularly important in child and adolescent samples, as attention control is still changing during this period, and may be more challenging to self-report.

Furthermore, whilst the ACS assesses an individual's general capacity to focus in the face of distraction and to shift attention, these capacities may differ from the ability to control attention in pain-specific contexts. In particular, individuals high in pain catastrophizing may exhibit more difficulties in attention control in pain than non-pain contexts. The fact that we find a significant moderation effect of general attention control attests to the importance of this general capacity in influencing pain-specific constructs, however examining attention control within the context of pain may further our understanding of this effect. Finally, this study is cross-sectional, so causal hypotheses are untested. Whilst pain catastrophizing may indeed impact attention bias to pain, the reverse may also be true. Indeed, according to a dual process framework, the interaction between attention bias and attention control may be useful in *predicting pain catastrophizing*. Given the hypothesized role of attention bias in the development and maintenance of chronic pain problems (Pincus & Morley, 2001), and the possibility of using attention bias modification techniques for prevention and intervention strategies (M. Dehghani et al., 2004; Sharpe et al., 2012), future studies employing longitudinal and training designs to investigate the dynamic interplay between attention biases, attention control, and pain catastrophizing will be valuable.

Finally, it will be important for future studies to consider not only the role of catastrophizing, but also pain-related fear and anxiety, within the context of pain-related

attending. Indeed, psychological models of chronic pain (e.g., (Vlaeyen & Linton, 2000)) posit roles for both catastrophizing as well as anxiety in the etiology of chronic pain. In addition, anxiety appears to be commonly comorbid with chronic pain disorders in youth (Campo et al., 2004; Chorney et al., 2011; Lipsitz et al., 2005), suggesting that it is important to examine the role of anxiety in pain-related vulnerability.

The current findings extend our understanding of the attentional functioning of adolescents with varying levels of pain catastrophizing. Our findings attest to the importance of attention control as a moderating variable on the association between pain catastrophizing and attention bias to pain, thus advancing theory and informing potential interventions.

Chapter 3

An edited version of this chapter has been published as follows:

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3

Adolescent Attention to Pain and Pain Tolerance are Dependent upon Anxiety and Attention Control: An Eye-Tracking Study

Pain is common and can be debilitating in childhood and adolescence. Theoretical models propose that attention to pain plays a key role in pain outcomes, however very little research has investigated this in youth. This study examined how anxiety-related variables and attention control interacted to predict adolescents' attention to pain cues using eye-tracking methodology, and their pain tolerance on the cold pressor test (CPT). Adolescents (and older children) aged 8-17 years had their eye-gaze tracked whilst they viewed photographs of other young people displaying painful facial expressions during the CPT, before completing the CPT themselves. Adolescents also completed self-report measures of anxiety, catastrophizing, and attention control. Findings indicated that anxiety and attention control did not impact adolescents' initial fixations on pain or neutral faces, but did impact how long they dwelled on pain versus neutral faces. For adolescents reporting low levels of attention control, higher anxiety was associated with *less* dwell time on pain faces as opposed to neutral faces, and the opposite pattern was observed for adolescents with high attention control. Anxiety and attention control also interacted to predict pain outcomes. For adolescents with low attention control, increasing anxiety was associated with anticipating more pain and tolerating pain for less time. This is the first study to examine adolescents' attention to pain cues using eye-tracking technology in the context of a salient painful experience. Data suggest attention control is an important moderator of anxiety on multiple outcomes relevant to young people's pain experiences.

3.1. INTRODUCTION

Affective-motivational models propose that pain imposes an attentional priority and motivates avoidance behaviour, particularly when one catastrophizes and is anxious about pain (Eccleston & Crombez, 1999; Vlaeyen & Linton, 2000). Relatedly, how one attends to pain, and subsequently engages in behaviour to avoid pain, is thought critical in the transition from acute to chronic pain. As pain often first becomes chronic in youth (Perquin et al., 2000), understanding the relationship between pain attending and pain-related anxiety and catastrophizing, as well as avoidance behaviour, is particularly important in paediatric populations (King et al., 2011). Paediatric research in this area is only beginning, yet both paediatric and adult literatures show conflicting findings, with some studies showing that increased anxiety and catastrophizing contribute to more pain attending and behavioural avoidance (Crombez et al., 1998; Heathcote et al., 2015; Van Damme et al., 2004; Verhoeven et al., 2010), whilst others provide null findings (Roelofs et al., 2003; Van Ryckeghem et al., 2012), or evidence counter to expectations (Boston & Sharpe, 2005; Vervoort et al., 2011, 2012). Understanding when anxiety and catastrophizing contribute to these outcomes is important for identifying those at risk for adverse pain experiences.

Attention control, the ability to focus effortfully in the face of distraction and flexibly shift attention, is likely important in understanding the variable relationship between pain-related anxiety and catastrophizing, and pain attending. Indeed, in Chapter Two we found that adolescents who catastrophize about pain, and have low attention control, showed high vigilance to pain facial expressions (Heathcote et al., 2015). However, whilst attention control provides one explanation for mixed findings, our results are preliminary, and outstanding questions remain.

Most studies have relied on paradigms that examine static measures of attention, indirectly via response times (e.g., the dot-probe task (J. E. Beck et al., 2011; Boyer et al., 2006; Vervoort, Trost, & Van Ryckeghem, 2013)). Eye-tracking methods alternatively provide continuous measures of attention over time. This may be particularly relevant in the context of effortful attention control, which is likely to have more pronounced effects on attention maintenance as opposed to initial selection. Further, most adult studies have relied on linguistic stimuli (pain words), which have low ecological validity and are indirectly related to pain. In Chapter Two, we employed pictorial stimuli (facial expressions of pain), but these stimuli were not personally relevant to participants' own pain experiences. A significant advance would be to use pictorial stimuli that relate to an impending pain experience (e.g., see (Vervoort, Trost, & Van Ryckeghem, 2013).

There are also conceptual considerations. Specifically, catastrophizing has been studied as the primary index of pain-related anxiety. However, affective-motivational models (Asmundson et al., 2012; Eccleston & Crombez, 1999; Van Damme et al., 2010; Vlaeyen & Linton, 2000) posit that general anxiety symptoms when facing pain also influence attention. Moreover, it has recently been argued that catastrophizing in childhood may be best understood as worry and anxiety about pain rather than catastrophic beliefs (Eccleston, Fisher, Vervoort, & Crombez, 2012). Therefore, examining broader anxiety symptoms, as well as catastrophizing, in young people's attending to pain is important. Further, while preliminary findings suggest attention control is important in understanding variable relationships between anxiety and attention, it remains unknown whether it has a similar moderating role on behavioural avoidance, which is considered key in explaining pain outcomes.

This study examines how anxiety and catastrophizing interact with attention control to predict adolescents' attention to pain cues, and their tolerance and experience of pain on the cold pressor test (CPT). Adolescents' eye movements were tracked whilst viewing photographs of other young people displaying painful facial expressions during the CPT, before completing the CPT themselves. We hypothesized that, particularly when attention control is low, high anxiety and pain catastrophizing would contribute to (1) increased attention towards pain cues, and (2) decreased tolerance of cold pressor pain, which can be thought of as an avoidance of further pain (Boston & Sharpe, 2005; Vervoort, Trost, & Van Ryckeghem, 2013).

3.2. METHODS

Participants

The majority of the participants were recruited from a sample of schoolchildren and adolescents (hereafter referred to as 'adolescents') (*N*=462) who participated in a questionnaire study about pain experiences that took place approximately five months previously (unpublished data). Only adolescents who had provided informed consent to be re-contacted were approached (*N*=136). Exclusion criteria for the current study were as follows: (1) recurrent or chronic pain, (2) developmental delay, (3) having insufficient knowledge of the Dutch language, and (4) not being between the ages of 8-17 years. From the total of 136 adolescents, 112 were contacted via their parents (the remaining did not provide contact details (*N*=10), or were younger or older than 8-17 years (*N*=14)). Of those contacted, 96.4% (*N* =108) met the inclusion criteria and 41.07% (*N*=46) agreed to participate. Thirty-two percent (*N*=36) refused to participate. The main reason for refusal to participate was "lack of time" or "other family responsibilities". The remainder of the adolescents (*N*=21) showed

initial interest in the study but were not contactable beyond the first time of contact (i.e., did not respond to a subsequent email or voicemail). To account for potential data loss during eye-tracking and to increase sample size, an additional nine adolescents were recruited via social media advertisement (advertisement was aimed at parents). There were no differences in anxiety, pain catastrophizing, and attention control between participants recruited via schools and those recruited via social media (all t (52) $\leq$ $\left|1.63\right|$, ns). As one of the participants recruited from the previous questionnaire study contributed as a pilot subject, the final sample of the present study consisted of 54 adolescents (and older children; age range 8-17 years, M=12.1 years, SD=2.39, 19 boys). Participants were compensated €30 for participating in this study. The study was approved by the Faculty of Psychology and Educational Sciences ethics committee, Ghent University, Belgium.

Apparatus

A cold pressor apparatus was used as an experimental pain task to induce pain in participants and to measure pain tolerance. Participants were instructed to lower their right hand into the cold water up to just above the wrist. Participants kept their hand in the cold pressor box up to their pain tolerance level or an uninformed ceiling of four minutes. The temperature of the water was maintained at 10°C (+/-1°C) and was circulated continuously by a pump (see also (Vervoort, Trost, & Van Ryckeghem, 2013)). The cold pressor apparatus is well suited for use with adolescents and the pain experienced is considered to provide an analogue for various naturally occurring acute pains (Birnie, Caes, Wilson, Williams, & Chambers, 2014; Von Baeyer, Piira, Chambers, Trapanotto, & Zeltzer, 2005). A second tank was also used, for which the water was maintained at room temperature (21°C; +/-1°C). To standardize skin temperature prior to cold pressor immersion, all participants first immersed

their hand in the room temperature water tank for a total of two minutes (see also (Birnie et al., 2014; Vervoort, Trost, & Van Ryckeghem, 2013). This procedure will henceforth be referred to as the Cold Pressor Test (CPT).

Pain tolerance

Pain tolerance was defined as the participant's total time of immersion in the cold water in seconds, measured by a stopwatch. Prior to the cold pressor test, participants were provided with the following instructions '*Hold your hand in the cold water as long as you can endure the pain. When you think/feel 'I cannot endure the pain any longer – I cannot handle more', I want you to say 'STOP' and take your arm out of the cold water box'.* The maximum duration of exposure to the CPT was four minutes. However, the participants were not informed of this ceiling so that there would be no risk that they mistakenly thought they were expected to leave their arm in the water for this length of time.

Self-report measures

Attention control

Attention control was assessed with the Dutch version of the Attention Control Scale (ACS) (Muris, Van Der Pennen, Sigmond, & Mayer, 2008). The ACS consists of 20 items, and yields a total score that can range from 20 to 80, with higher scores indicating good attention control. The ACS has two subscale scores for attention focusing (e.g., *"My concentration is good even if there is music in the room around me"*) and attention shifting (e.g., *"It is easy for me to alternate between two different tasks"*). The ACS has shown both good reliability and predictive utility, predicting resistance to interference in Stroop-like spatial conflict tasks as well as attentional disengagement from threat stimuli among highly

anxious people (Derryberry & Reed, 2002). Attention control has also been measured with good reliability and validity in children and adolescents (Heathcote et al., 2015; Meesters, Muris, & Van Rooijen, 2007). Cronbach's alpha in this study was .67 for the total score.

State anxiety

State anxiety was assessed by the State version of the Dutch *State-Trait Anxiety Inventory for Children* (STAIC-state) (Bakker, Van Wieringen, Van der Ploeg, & Spielberger, 1989; Spielberger, Edwards, Lushene, Montuori, & Platzek, 1973). The STAIC-state is a 20-item questionnaire designed to measure current anxious state in young people. Participants are presented with various emotions (e.g., calm, nervous) and asked to read each item and to decide how they feel "right now." Each item consists of a statement beginning "*I feel*….", and ending with three possible emotional states (e.g., '*very calm*', '*calm*' or '*not calm*'). Total scores can range from 0 to 40. The decision to measure state rather than trait anxiety was based on previous findings indicating that state anxiety is usually highly correlated with trait anxiety and is likely to be a more proximal predictor of participants' situational responses (see also (Vervoort, Trost, Sütterlin, Caes, & Moors, 2014)). Furthermore, we were interested in state anxiety symptoms in the face of an upcoming painful experience (the CPT), making the measure relevant within the context of pain. The STAIC-state has been shown to be a reliable and valid instrument in previous research (see (Bakker et al., 1989; Spielberger et al., 1973)). Cronbach's alpha in this study was .74.

Catastrophic thinking about pain

A situation-specific measure based upon the original Pain Catastrophizing Scale for Children (PCS-C; (Crombez et al., 2003)) was administered to measure the participants'

catastrophizing thoughts about the upcoming pain task. Again, we were interested in state catastrophizing in the face of an upcoming painful experience (the CPT), making the measure relevant for this healthy sample, and more relevant for the outcome of pain tolerance. The original PCS-C consists of 13 items describing different thoughts and feelings that young people may experience when they are in pain, and yields three subscale scores for rumination, magnification, and helplessness. The PCS-C has shown to be a reliable and valid instrument in young people from 9 to 15 years (Crombez et al., 2003). The use of a situation-specific measure of catastrophizing, i.e., assessing the level of catastrophizing thoughts about an upcoming pain task, is consistent with previous studies (Vervoort, Goubert, & Crombez, 2009). The situation-specific measure of the PCS-C consists of two adapted items from each subscale (Rumination: *"At this moment, to what extent do you keep thinking about how much pain you will experience during the test?"*; Magnification: *"At this moment, to what extent do you think that, because of the pain, something serious might happen to you?"*; Helplessness: "*At this moment, to what extent do you think you will not be able to endure the test because of the pain?"*). The six items of the situation-specific PCS-C were rated on an 11-point numerical rating scale (0 = 'not at all'; 10 = 'very much'), and were completed before the attention task (i.e., eye-tracking task). The total score on catastrophizing could range from 0 to 60 and was used as an index of the participant's catastrophizing thoughts about anticipated pain. Cronbach's alpha in this study was .81.

Anticipated and experienced pain intensity

Anticipated and experienced pain intensity during the cold pressor test were assessed using 11-point 1-item scales with the anchors 'no pain' (0) and 'a lot of pain' (10). Participants were requested to provide written ratings for these measures immediately before

and after completing the CPT. For the current study, the participant's self-reported anticipated and experienced pain intensity were considered secondary outcome measures (pain tolerance was the primary outcome of interest).

Stimulus materials

The stimulus set for the viewing task consisted of 40 grey-scaled pictures of 10 different children (5 boys and 5 girls; age range 9-16 years) displaying neutral and pain facial expressions. These pictures were previously used in a dot-probe study in children and an eye-tracking study in parents examining child and parental attention to child pain, respectively (see (Vervoort et al., 2014; Vervoort, Trost, & Van Ryckeghem, 2013)). These pictures were previously reliably coded for occurrence and intensity of facial pain display by means of the Child Facial Coding System (CFCS) (Christine T Chambers, McGrath, Gilbert, & Craig, 1996). For each of the 10 children in the stimulus set, four pictures were chosen to reflect each of four categories of facial pain expression: one picture of a particular child depicted the child's neutral face (NFE); one picture depicted the child with a low pain facial expression (LFE); one showed a moderate pain facial expression (MFE), and one depicted a high pain facial expression (HFE). Using the 40-picture set, three types of picture pairings were generated, resulting in 30 slides. Specifically, each slide consisted of two pictures of the same child presenting a neutral expression combined with the same child's low pain, moderate pain, or high pain expression. This allowed examination of whether participants' selective attention to pain faces varied with varying levels of facial pain expressiveness. Pairs were compiled twice such that the neutral expression appeared equally often on the left and right side (i.e., 60 slides were shown: 20 neutral-low pain; 20 neutral-moderate pain, and 20 neutral-high pain). The validity of the present stimulus set is supported by previous findings

that differential facial pain expressiveness (i.e., NFE, MFE, LFE, HFE) reflects differences in observers' pain intensity ratings such that increasing levels of facial pain expressiveness corresponded with observers' increasing pain ratings (see (Vervoort, Trost, Prkachin, et al., 2013; Vervoort, Trost, & Van Ryckeghem, 2013)).

Eye movement measurement

Eye movements were tracked with a 300 Hz Tobii (TX300) table-mounted eye tracker (Tobii Technology AB, Danderyd, Sweden). This system consists of a 17-inch computer screen with a camera and infrared LED optics embedded beneath it. The system records eye movements based on the corneal reflection caused by the infrared light source. Participants were seated comfortably 60cm away from the centre of the screen. In order to calibrate the eye-tracker, participants were asked to focus on nine sequentially appearing red dots presented in random placement on the screen. The viewing task commenced after valid calibration.

Free-viewing (eye-tracking) task

Participants were informed that they would complete a viewing task, in which their eye movements would be tracked. Participants were informed that during the task, they would view photographs of other young people on the screen. To make the stimuli salient and related to a personal painful experience, participants were told that these photographs represented young people undergoing the CPT (i.e., the painful task that that they would subsequently perform). Participants were shown an overview of one trial (on paper) in order to ensure familiarity with the experimental set up. Participants were instructed to first focus on a centrally-presented white fixation cross when it appeared on screen and then to simply

view the faces that would subsequently appear on the screen. Each trial within the viewing task began with a 500ms presentation of the white fixation cross. Then, a slide with the pair of facial stimuli against a grey background was presented for 3500ms and participants were free to visually explore the slide. Following an inter-trial interval of 200ms (grey screen), the next trial again began with the presentation of the fixation cross. In total, the experiment consisted of 60 trials: each of the 30 slides was presented twice, once with the pain face on the left and once on the right side of the screen. Pictures were 16cm high and 10cm wide. Pictures were separated by 4.4 cm from their central points. Slides were presented to participants in a fully randomized order.

Picture pain intensity ratings

After completing the viewing task, participants were asked to rate each presented pain face for pain intensity using a 0-10 NRS (i.e., 'How much pain has the child displayed on the picture; anchors; 'no pain at all'; 'a lot of pain'). Pictures were presented on a computer screen using Office PowerPoint in a randomized order that was fixed across participants. Participants were instructed to make written ratings of pain intensity for all pictures and were encouraged to proceed as fast as possible. Picture ratings were averaged for each level of facial pain display (NFE, LFE, MFE, HFE) resulting in four mean pain intensity ratings ranging from 0-10. This allowed examining whether differences in facial expressiveness of the pictures matched differences in the participant pain intensity ratings of the pictures.

Procedure

All participants were invited by telephone and received standardized information about the study. When parents and their children provided consent, they were invited to the

laboratory at Ghent University where the study was conducted (In July 2014 and August/September 2014). Upon arrival at the laboratory, one of two experimenters (both female) accompanied the parent and their child to the test-room. They were were told that the child would perform a computerized eye-tracking task (i.e., the free-viewing task), and complete a number of questionnaires. Furthermore, the cold pressor apparatus was shown to the parent and their child, and they were told that the child could remove their arm from the water at any time, for any reason, and that the child could withdraw from participation at any time.

After obtaining written parental and child consent, Experimenter One stayed with the participant in the test-room while Experimenter Two accompanied the parent to an adjacent room. Before performing the free-viewing task, participants were requested to fill out measures on attention control, state anxiety, and state pain catastrophizing. Participants completed these measures before the free-viewing task as we were primarily interested in their baseline emotional response when entering the lab and beginning the study, and because we aimed to examine the influence of these baseline measures on subsequent attention. Participants then completed the free-viewing task. As noted above, to make the stimuli salient and related to a personal painful experience, participants were told that these photographs represented children undergoing the CPT, the painful task that they would subsequently perform. Following the viewing task, the participant's pain tolerance was assessed during the CPT. Participants' anticipated and experienced pain for and during the CPT were assessed before and after they completed the task, respectively. Participants and parents could not see or hear each other throughout the duration of the study procedure. In addition, to prevent any contact between the experimenter and the participant, the experimenter was seated silently behind a screen during performance of the cold pressor test. After completion of the entire

study procedure, parent-child dyads were reunited in the test-room and were fully debriefed about the purpose of the study.

Eye movement parameters and data analysis

Gaze behaviour was analyzed off-line with the Tobii software analysis package (Tobii Studio 3.2) using the Identification Velocity-Threshold (I-VT) filter (classifier: 30°/s; Velocity calculator window length: 20 ms). The minimum fixation duration was set at 100ms. The I-VT fixation classifier is based on the Velocity-Threshold identification fixation filter as described by Salvucci and Goldberg (Salvucci, Salvucci, Goldberg, & Goldberg, 2000) and Komogortsev et al (Komogortsev, Gobert, Jayarathna, Koh, & Gowda, 2010). Within the present study, the two target pictures were defined as areas of interest (AOIs) within which eye movements would be monitored. Two eye movement parameters were calculated: (1) probability of first fixation, and (2) total fixation duration. Probability of first fixation refers to whether or not participants first fixated their attention on the pain face or the neutral face. A 'first fixation bias' refers to a higher probability of the participant to first fixate on the pain face rather than the neutral face. Accordingly, first fixation bias was calculated by computing the number of trials when the first fixation was directed on the pain face as a proportion of all trials in which the first fixation was made to either face (proportion scores >0.5 reflect an orienting bias toward pain faces; 0.5 = no bias; <0.5 reflect an orienting bias toward neutral faces). This was done separately for each facial pain expression category (LFE, MFE, HFE), resulting in 3 probability indices of first fixation bias. Total fixation duration for each facial expression was generated by averaging the total time participants spent looking at faces for each facial expression category separately (NFE, LFE, MFE, HFE). A 'total fixation bias' refers to when a participant spends longer looking at pain faces rather than neutral faces. In

the current study (as in previous studies), total fixation duration may also be referred to as "dwell time".

To examine the impact of participant anxiety, pain catastrophizing, and attention control upon attention to pain, a series of repeated measures analyses of covariance (ANCOVA) were performed for each of the eye movement indices (i.e., probability of first fixation and total fixation duration) with facial expressiveness as a within subject factor and attention control and anxiety or pain catastrophizing entered as covariates, respectively, in separate analyses. To examine the impact of anxiety, pain catastrophizing, and attention control upon pain tolerance, univariate analyses of covariance (ANCOVAs) were performed with pain tolerance as the dependent variable and attention control and anxiety or pain catastrophizing entered as covariates, respectively, in separate analyses. Additional analyses were also performed with anticipated and experienced pain intensity during CPT performance as the dependent variable, as this was considered a secondary outcome within the present study.

Continuous predictor variables (anxiety/pain catastrophizing/attention control) were centered prior to entering the analyses. Centering reduces the multicollinearity between predictors and any interaction terms among them and facilitates post-hoc probing of significant interaction effects (Holmbeck, 2002). Further, in case the analyses with total fixation duration revealed significant interactions with facial expressiveness, bias indices ('total fixation bias') were calculated to further aid interpretation of direction of effects. Separate total fixation bias scores were calculated for each level of facial pain expressiveness (HFE, MFE, LFE). In these analyses, positive values of total fixation bias (i.e., mean total dwell time on pain faces subtracted from mean total dwell time on neutral faces) indicated that dwell time on pain faces was higher than dwell time on neutral faces, whereas a negative

score indicated the reverse: higher dwell time on neutral faces. ANCOVA was performed on these bias indices.

In case of significant interactions, additional moderation analyses were performed to interpret the interaction effects (i.e., whether the association between the predictor variable and the outcome was significant only for high levels of the moderator variable, low levels of the moderator variable, or both). All moderation analyses followed the procedure outlined by Holmbeck et al. (Holmbeck, 2002), i.e., two new conditional continuous moderator variables were computed by (1) subtracting one SD from the centered moderator variable (high attention control) and (2) adding one SD to the centered moderator variable (low attention control). Next, two additional ANCOVAs were performed - incorporating each of these new conditional continuous moderator variables - to test the significance for high (+1 SD above the mean) and low (-1 SD below the mean) values of the conditional centered moderator variable. To fully understand observed interactions, additional moderation analyses were run to examine the impact of attention control upon attention to pain as a function of low versus high levels of anxiety and catastrophizing, respectively, using a similar moderation procedure as outlined above (Holmbeck, 2002). Whenever the sphericity assumption was violated (Mauchly's test of sphericity was $p < .05$), Greenhouse-Geisser corrections (with adjusted degrees of freedom, or NDf) were performed. Bonferroni correction for multiple comparisons was not appropriate as the current study did not meet any of the conditions for applying this adjustment (i.e., (a) a universal null hypothesis is of interest, (b) the same test is repeated in many subsamples, (c) searching for significant associations without a priori hypotheses for multiple tests) (Perneger, 1998). Effect sizes were reported using the Partial Eta Squared index (η_p^2). Following Cohen (Cohen, 1988) and Oleknik and Algina (Olejnik & Algina, 2000); small effect size = 0.01; medium effect size = 0.06; large effect size = 0.14.

3.3. RESULTS

Participant characteristics

Data from 17 participants were discarded from analyses due to sub-optimal overall gaze track status (i.e., eye movements tracked less than 70% of total task viewing time). This is in line with previous eye-tracking studies (Vervoort, Trost, Prkachin, et al., 2013). The final sample entered in all of the analyses reported below therefore consisted of 37 adolescents (14 boys) aged 8-17 years (*M*=12.1 years, *SD*=2.45). Those participants whose data were discarded did not differ from the participants retained in the analysis on any of the independent or dependent measures (all $t\ (52) \leq |1.58|$, ns). Mean scores, standard deviations, and correlations between measures are reported in Table 3.1. The mean level of state anxiety (*M*=12.2; *SD*=5.48), pain catastrophizing (*M*=15.8; *SD*=10.0), and attention control (*M*=33.3; *SD*=6.06) in the present sample are comparable with those obtained in previous samples of school youths (Bakker et al., 1989; Muris et al., 2008; Vervoort et al., 2009). Participants reported moderate levels of anticipated (*M*=4.05; *SD*=2.21) and experienced mean pain intensity (*M*=5.00; *SD*=2.05) during CPT performance. Participants' CPT immersion time ranged from 18 to 240 seconds with a mean of 124.4 s (*SD*=99.1). Participants' pain tolerance in the current study is therefore in line with previous studies (Vervoort, Trost, & Van Ryckeghem, 2013). About two third of the participants (59.5 %) withdrew their hand from the cold water before the four minute ceiling was reached.

Pearson correlation analyses indicated that self-report measures and pain tolerance did not correlate significantly with participant age (all $r \leq \left| .05 \right|$, ns). There were no significant differences between girls and boys for any of the measures (all $t(35) \leq \left| 1.00 \right|$, ns), except for anticipated and experienced pain intensity which was higher amongst girls (both $t(35) \leq -2.22$, $p<.05$). State anxiety was significantly correlated with state pain catastrophizing ($r=.41$,

p<.05). State anxiety and state pain catastrophizing were not significantly correlated with attention control (*r* = -.12 and -.20, respectively, ns), and none of these measures correlated with pain tolerance (all $r \leq |.27|$, ns). However, both the participant's anticipated and experienced pain intensity during CPT were significantly correlated with state pain catastrophizing (both *r*≥.38, *p*<.05). Experienced pain intensity was also significantly negatively correlated with pain tolerance (*r*= -.34, *p*<.05).

Table 3.1: *Means (M), standard deviations (SD) and Pearson correlation coefficients for all self-report measures, pain intensities, and pain avoidance*

	Range	*M*	*SD*	1	2	3	4	5	6
1. State pain catastrophizing	0-36	15.81	10.04	---	.41*	-.20	.57***	.38*	.27
2. State anxiety	5-29	12.20	5.48		---	-.12	.25	.05	.08
3. Attention control	21-43	33.32	6.06			---	.01	-.02	-.01
4. Anticipated pain intensity	0-8	4.05	2.21				---	.55**	.25
5. Experienced pain intensity	2-9	5.00	2.05					---	.37*
6. Pain avoidance	0-222	115.59	99.13						---

*p < .05; **p < .01; ***p < .0001

Picture ratings

In order to examine whether the different picture categories of facial pain expressiveness matched differences in the participant's ratings of pain intensity (therefore to confirm stimulus categories), participants' pain intensity ratings of the pictures were examined using a repeated measures ANOVA. Results revealed significant differences between ratings of the four expression levels ($F(3,34)=309.4$, $\epsilon=.66$; NDf(1.98;22.44), *p*<.0001). Differences were in the expected direction. Specifically, contrasts revealed that high expressive pain faces (*M*=68.4 *SD*=15.6) were rated significantly higher than moderate expressive pain faces (*M*=55.4; *SD*=14.5; $F(1,36)=160.66$, *p*<.0001) which, in turn, were rated significantly higher than low expressive pain faces (*M*=44.4; *SD*=14.9; $F(1,36)=82.6$, *p*<.0001) which, in turn, were rated significantly higher than neutral faces (*M*=29.0; *SD*=15.9;

$F(1,36)=243.4$, $p<.0001$). Adding either anxiety or pain catastrophizing, respectively, as a covariate to the repeated measures ANOVA revealed no main effects or interactions effects (all $F(1,35)\leq.2.40$, ns).

The impact of anxiety and pain catastrophizing upon attention to pain, and the moderating role of attention control

Probability of first fixation

We first investigated whether or not participants first fixated on pain faces significantly more than neutral faces (i.e., whether or not there was an overall first fixation bias). As a primary repeated measures ANOVA revealed that there were no significant differences between first fixation bias towards low (M=.53), medium (M=.53), and high expressive pain faces (M=.52) ($F(2,35)=.07$, ns, $\eta_p^2 = 0.002$), we calculated a mean first fixation bias score across all three pain expressions. A one-sampled t-test revealed a mean first fixation bias (M=.53) significantly greater than chance (.50) indicating that participants first fixated significantly more on pain faces than neutral faces ($t(36)=3.30$, $p<.005$).

To investigate the impact of *anxiety* and the moderating role of *attention control* upon the participant's first fixation bias, a repeated measures ANCOVA was performed with anxiety and attention control entered as covariates. Analysis indicated no main or interaction effects for anxiety, attention control, and/or facial expressiveness (all $F\leq1.06$, ns, all $\eta_p^2 < 0.03$).

The analysis examining the impact of *pain catastrophizing* and the moderating role of *attention control* revealed no main or interaction effects for pain catastrophizing, attention control, and/or facial expressiveness (all $F \leq 1.43$, ns, all $\eta_p^2 < 0.001$).

Total fixation duration

We first investigated whether or not participants dwelled longer on pain faces compared to neutral faces (i.e., whether or not there was an overall total fixation bias to pain). A repeated measures ANOVA with facial expressiveness as a within-subject factor (i.e., dwell time on neutral, low pain, moderate pain, and high pain faces) revealed a significant effect ($F(3,34)=17.17$; $\epsilon=.61$; NDf(1.83;20.74), $p<.0001$, $\eta_p^2 = 0.33$). Contrasts revealed that dwell time on pain faces significantly increased with each level of pain expressiveness (i.e., $M_{TFD_lowpain}=1.28$s; $M_{TFD_modpain}=1.34$s, $M_{TFD_highpain}=1.39$s) and was significantly longer compared to dwell time on neutral faces ($M_{TFD_neutral}=1.08$s; all $F(1,36) \geq 17.51$, $p<.0001$).

Adding *anxiety* and *attention control* as covariates to the repeated measures analysis indicated a significant anxiety x attention control x facial expressiveness interaction ($F(3,30)=3.65$, $\epsilon=.62$; NDf(1.86;18.6), $p<.05$, $\eta_p^2 = 0.10$). This indicates that the interaction between anxiety and attention control is different depending on the type and/or level of facial expressiveness (ie., neutral expression, low pain expression, moderate pain expression, and high pain expression). To interpret this significant interaction, we first calculated total fixation bias scores for each level of pain facial expression (i.e., the degree to which participants dwelled on low, moderate, and high pain expressions in comparison to neutral faces). Using these total fixation bias indices, we performed a repeated measures ANCOVA with total fixation bias indices for LFE, MFE, and HFE as dependent variables and attention

control and anxiety as covariates. Findings indicated a significant anxiety x attention control interaction (F(,33) =4.84, p<.05, η_p^2 = 0.20). No significant anxiety x attention control x facial expressiveness interaction (F(2,32) =1.75, ns, η_p^2 = 0.11) was observed, indicating that total fixation bias indices were not different for low, moderate, or high pain facial expressiveness. Accordingly, two univariate ANCOVAs were conducted with the *mean total fixation bias* (i.e., dwell time averaged across low, moderate, and high expressive pain faces) to further interpret differences for anxiety between participants who reported high levels of attention control and those who reported low levels of attention control. As shown in Figure 1.1, findings indicated a cross-over interaction signifying that anxiety differentially impacted the participant's dwell time on pain faces depending upon the participant's level of attention control. Specifically, for participants reporting high levels of attention control, higher anxiety was associated with *increasing* dwell time on pain faces (Low anxiety: M = 0.01 seconds, High anxiety: M = 0.3 seconds). Conversely, for participants reporting low levels of attention control, higher anxiety was associated with *decreasing* dwell time on pain faces (Low anxiety: M = 0.49 seconds, High anxiety: M = 0.29 seconds). While these patterns did not significantly differ from 0 for participants reporting low attention control (F(1,33)=1.69, ns, η_p^2 = 0.05) and only approached significance for participants reporting high attention control (F(1,33)=3.96, p=.06, η_p^2 = 0.11), the significant cross-over interaction indicates that these patterns are significantly different from each other. Furthermore, as shown in Figure 1.1 (dotted lines), findings suggest that attention control has the most impact at lower levels of anxiety. Indeed, additional analyses indicated that for participants with low levels of anxiety, increasing attention control is associated with decreasing dwell time on pain faces

($F(1,33)=9.28$, $p<.005$, $\eta_p^2 = 0.22$). Attention control is not associated with dwelling on pain faces at high levels of anxiety ($F(1,33)=.002$, ns, $\eta_p^2 = 0.00$).

Similar analysis but with pain catastrophizing entered as a covariate instead of anxiety indicated that the expected three-way interaction (i.e., catastrophizing x attention control x facial expressiveness) failed to reach significance ($F(3,31)=1.93$, $\epsilon=.62$; NDf(1.86;19.22), ns, $\eta_p^2 = 0.06$). This suggests that the interaction between attention control and pain catastrophizing did not impact dwell time differently for neutral faces or pain faces (at any level of pain expressiveness). Analyses only revealed a significant attention control x facial expressiveness interaction ($F(3,31)=4.69$, $\epsilon=.62$; NDf(1.86;19.22), $p<.05$, $\eta_p^2 = 0.12$) and an attention control x pain catastrophizing interaction ($F(1,33)=4.87$, $p<.05$, $\eta_p^2 = 0.13$). The former two-way interaction (i.e., attention control x facial expressiveness) is not explored further since previous analyses indicated that this two-way interaction is subsumed by a three-way interaction between anxiety, attention control, and facial expressiveness.

To interpret the significant pain catastrophizing x attention control interaction, separate ANCOVAs were performed for participants reporting low and high attention control, respectively, and mean dwell time (averaged across the four expressiveness levels) entered as the dependent variable. As shown in Figure 1.2, findings indicated that pain catastrophizing was positively associated with overall dwell time (on all faces) at high levels of attention control (Low catastrophizing: $M = 1.18$ seconds, High catastrophizing: $M = 1.32$ seconds) but negatively associated with overall dwell time (on all faces) at low levels of attention control (Low catastrophizing: $M = 1.37$ seconds, High catastrophizing: $M = 1.29$ seconds). While neither of these patterns reached significance (both $F(1,33)\leq 2.32$ ns, both $\eta_p^2 < 0.07$), the significant cross-over interaction suggests associations are significantly different from each

other. As shown in Figure 1.2 (dotted lines), findings suggest that attention control has the most impact at lower levels of pain catastrophizing. Indeed, additional analyses indicated that attention control is significantly negatively associated with overall dwell time (i.e., to all face types) at low levels of pain catastrophizing ($F(1,33)=5.59$, $p<.05$, $\eta_p^2 = 0.15$). Attention control is not associated with overall dwell time at high levels of pain catastrophizing ($F(1,33)=.38$, ns, $\eta_p^2 = 0.01$).

In sum, eye movement analyses indicated that participants overall first fixated on pain faces more than neutral faces, and dwelled longer on pain faces than neutral faces. Whilst there was no impact of psychological variables (i.e., anxiety, pain catastrophizing, or attention control) on first fixations, psychological variables did modulate dwell time on pain versus neutral faces, particularly within the context of anxiety and attention control. Specifically, anxiety differentially impacted the participant's dwell time on pain faces depending upon the participant's level of attention control. Whilst the association between pain catastrophizing and attention control was predictive of dwell time on all faces (i.e., looking for longer at all faces, regardless of face type or level of expressiveness), pain catastrophizing was not associated with biased attentional processing of pain, even when attention control was taken into account.

The impact of anxiety and pain catastrophizing upon pain outcomes, and the moderating role of attention control

Pain tolerance

The analysis investigating the impact of *anxiety* and the moderating role of *attention control* upon the participant's pain tolerance (i.e., the participant's total immersion time during the cold pressor test) revealed a significant anxiety x attention control interaction ($F(1,33)=6.49$, $p<.05$, $\eta_p^2 = 0.16$), indicating that the impact of anxiety upon tolerance is dependent upon the participant's level of attention control. Separate ANCOVAs for participants with high and low attention control indicated a cross-over interaction (see Figure 1.3). Similar to our findings on the impact of anxiety upon attentional maintenance to pain as a function of low vs. high attention control, findings indicated that the impact of anxiety upon pain tolerance shows opposite patterns depending upon low vs. high levels of attention control. Specifically, in line with expectations, findings indicated that higher levels of anxiety were associated with lower pain tolerance amongst participants reporting *low* levels of attention control (Low anxiety: M = 189.91 seconds, High anxiety: M = 80.75 seconds) ($F(1,33)=5.13$, $p<.05$, $\eta_p^2 = 0.14$). The opposite (but non-significant) pattern was found for participants reporting high levels of attention control (Low anxiety: M = 88.67 seconds, High anxiety: M = 160.01 seconds) ($F(1,33)=2.32$, ns, $\eta_p^2 = 0.07$). Furthermore, additional analyses (see Figure 1.3; dotted lines) indicated that attention control exerts opposite effects depending on whether participants are lowly or highly anxious. Specifically, for participants with low levels of anxiety, increasing attention control is associated with decreasing pain tolerance ($F(1,33)=4.02$, $p=.05$, $\eta_p^2 = 0.11$). The opposite (but non-significant) pattern was found for participants reporting high levels of anxiety ($F(1,33)=3.16$, ns, $\eta_p^2 = 0.09$). The

analyses with *pain catastrophizing* and *attention control* revealed no significant main or interaction effects (all $F \leq 2.40$, ns, all $\eta_p^2 < 0.07$).

Anticipated and experienced pain intensity

The analyses with *anxiety and attention control* as independent variables and *anticipated* pain intensity as the dependent variable revealed a significant anxiety x attention control interaction ($F(1,33)=7.29$, $p<.05$, $\eta_p^2 = 0.18$). Separate ANCOVAs for participants with high and low attention control indicated a crossover interaction (see Figure 1.4). Resembling findings on the impact of anxiety x attention control upon attentional maintenance to pain as well as pain tolerance, findings indicated that the impact of anxiety upon anticipated pain again shows opposite patterns depending upon low vs. high levels of attention control. Specifically, findings indicated that higher levels of anxiety were associated with higher anticipated pain amongst participants reporting *low* levels of attention control (Low anxiety: $M = 2.14$, High anxiety: $M = 5.32$) ($F(1,33)=9.63$, $p<.005$, $\eta_p^2 = 0.23$). Findings at *high* levels of attention control showed the opposite pattern but failed to reach significance (Low anxiety: $M = 4.57$ seconds, High anxiety: $M = 3.69$ seconds) ($F(1,33)=.38$, ns, $\eta_p^2 = 0.02$). Furthermore, additional analyses (see Figure 1.4; dotted lines) indicated that attention control exerts opposite effects depending on whether participants are lowly or highly anxious. Specifically, for participants with low levels of anxiety, increasing attention control is associated with increasing anticipation of pain intensity ($F(1,33)=5.11$, $p<.05$, $\eta_p^2 = 0.13$). Findings at high levels of anxiety showed the opposite pattern but failed to reach significance ($F(1,33)=3.00$, ns, $\eta_p^2 = 0.08$). The analysis with *experienced* pain intensity as

dependent variable revealed no significant main or interaction effects (all $F(1.33) < .59$, ns, all $\eta_p^2 < 0.02$).

The analyses with *pain catastrophizing and attention control* for both anticipated and experienced pain intensity only revealed significant main effects for pain catastrophizing such that higher levels of pain catastrophizing were associated with higher anticipated and experienced pain intensity (both $F(1.33) \geq 6.26$, $p < .05$, $\eta_p^2 = 0.31$ and 0.16 respectively). There were no other significant main or interaction effects (all $F(1.33) \leq 3.06$, ns, all $\eta_p^2 < 0.09$).

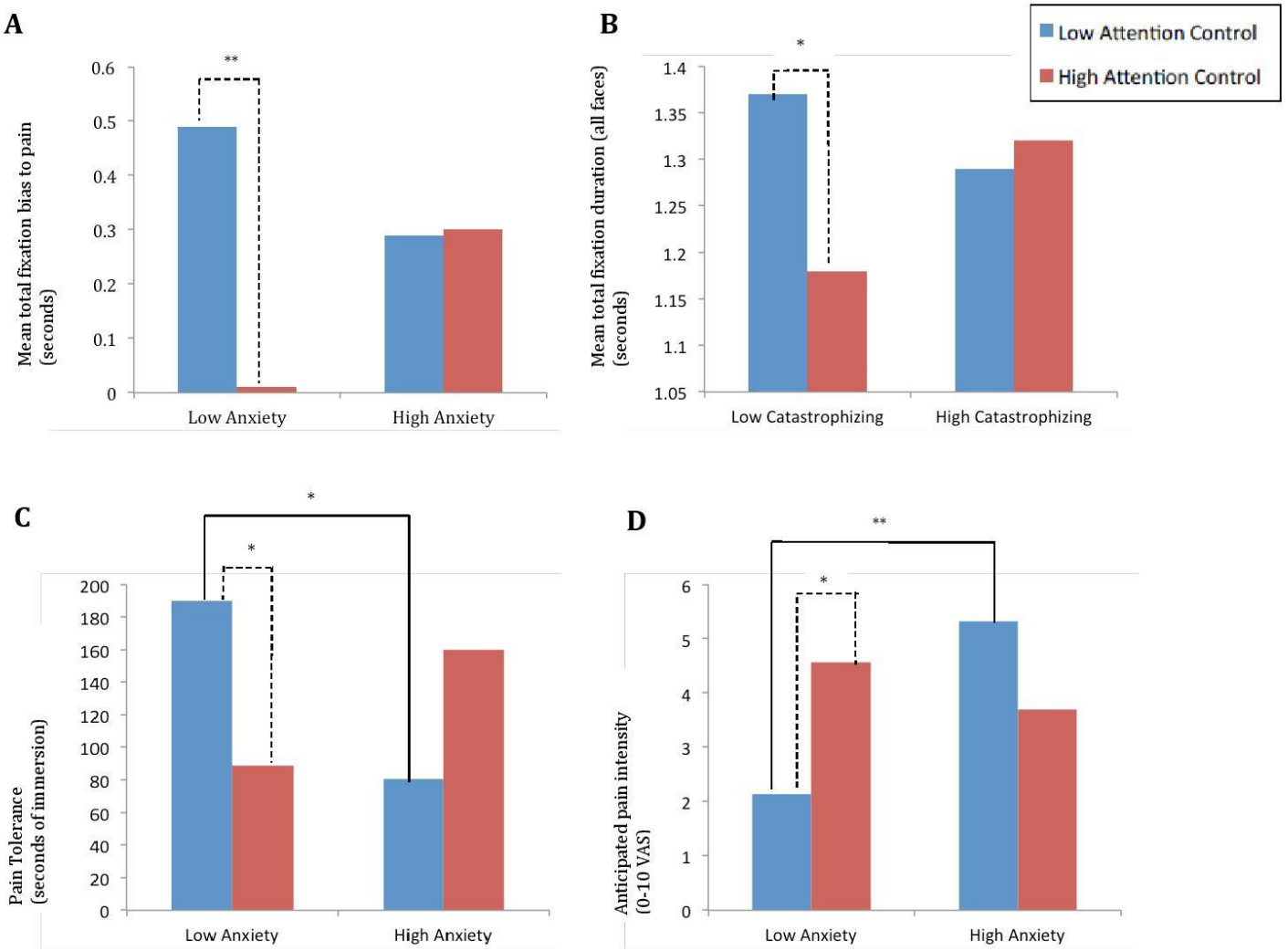

A
Mean total fixation bias to pain (seconds)
0.6
0.5
0.4
0.3
0.2
0.1
0
**
Low Anxiety
High Anxiety
B
Low Attention Control
High Attention Control
Mean total fixation duration (all faces) (seconds)
1.4
1.35
1.3
1.25
1.2
1.15
1.1
1.05
*
Low Catastrophizing
High Catastrophizing
C
Pain Tolerance (seconds of immersion)
200
180
160
140
120
100
80
60
40
20
0
*
*
Low Anxiety
High Anxiety
D
Anticipated pain intensity (0-10 VAS)
6
5
4
3
2
1
0
**
*
Low Anxiety
High Anxiety

Figure 3.1

(1) Mean total fixation bias to pain cues (averaged across low, moderate, and high facial pain expressiveness) as a function of low (1 SD below the mean) and high (1 SD above the mean) levels of adolescents' anxiety and attention control

(2) Mean total fixation duration (averaged across all faces) as a function of low (1 SD below the mean) and high (1 SD above the mean) levels of adolescents' anxiety and attention control.

(3) Pain tolerance (in seconds) as a function of low (1 SD below the mean) and high (1 SD above the mean) levels of adolescents' anxiety and attention control.

(4) Anticipated pain intensity as a function of low (1 SD below the mean) and high (1 SD above the mean) levels of adolescents' anxiety and attention control.

All: **$p \leq .005$; *$p \leq .05$

3.4. DISCUSSION

This study examined how anxiety-related variables and attention control interacted to predict adolescents' attention to visual pain cues, and their tolerance of pain on the cold pressor test (CPT). Furthermore, we also explored relationships with anticipated and experienced pain intensity. Adolescents' eye movements were tracked whilst viewing photographs of other young people displaying painful facial expressions during the CPT, before completing the CPT themselves. We hypothesized that, particularly when attention control is low, high anxiety and pain catastrophizing would contribute to (1) increased attention towards pain cues, and (2) decreased tolerance of cold pressor pain, which can be thought of as an avoidance of further pain (Boston & Sharpe, 2005; Vervoort, Trost, & Van

Ryckeghem, 2013). Results were in line with expectations regarding cold pressor pain outcomes, and partially in line with expectations regarding attention.

Regarding attention; anxiety, pain catastrophizing, and attention control had no effect on where adolescents first fixated their attention. That is, irrespective of anxiety or attention control, adolescents tended to first fixate on pain faces as opposed to neutral faces. Adolescents also tended to dwell for longer on pain faces than neutral faces (and increasingly longer on highly expressive pain faces). However, dwell time on pain faces was dependent upon anxiety, moderated by attention control. Specifically, anxiety showed *opposite* relationships with dwell time depending upon whether adolescents reported low or high levels of attention control, but with findings in the opposite direction than expected. Specifically, for adolescents reporting low levels of attention control, higher anxiety was associated with *decreasing* dwell time on pain faces (although adolescents still overall attended more towards pain than neutral faces, suggesting there was no avoidance of pain faces). Conversely, for adolescents reporting high levels of attention control, higher anxiety was associated with *increasing* dwell time on pain faces as opposed to neutral faces. While these patterns of anxiety and pain attending did not significantly differ from zero for participants reporting low attention control, and only approached significance for participants reporting high attention control, the significant cross-over interaction indicates that these patterns are significantly different from each other. Regarding cold pressor pain outcomes; attention control played a similar moderating role. That is, at *low* levels of attention control, adolescents with increasing anxiety anticipated more pain and were less tolerant for pain. The opposite pattern (though not significant in itself) was observed for adolescents with high levels of attention control. Thus, all three analyses with anxiety and pain attending, anticipation, and tolerance showed similar cross-over interactions, indicating a robust

moderating role of attention control across self-report and behavioural outcomes. Our findings therefore suggest that when an adolescent is increasingly anxious in the face of pain, low attention control is important in understanding worse pain outcomes. Further, our findings replicate those within the anxiety literature, demonstrating that attention control moderates the association between anxiety and attending towards threatening stimuli (Bardeen & Orcutt, 2011; Derryberry & Reed, 2002; Helzer et al., 2009; Schoorl et al., 2014; Susa et al., 2012).

However, it is intriguing that our findings regarding pain attending were in the opposite direction than expected, with higher anxiety associating with increasing dwell time on pain faces for adolescents reporting *high,* not low attention control. One possible but highly tentative explanation for these findings is that increased attending to pain cues, facilitated by high attention control, can be conceived of as a strategy employed by increasingly anxious adolescents that may have enabled them to seek further information about the upcoming painful experience, thus allowing re-appraisal. Accordingly, the observed pattern may reflect effective use of emotion regulation, in which attending to information about upcoming pain allows the regulation of aversive emotions (such as anxiety) by being able to focus on and re-appraise the threatening nature of pain. Whilst this suggestion certainly requires independent exploration, there is indeed previous evidence that adults who are highly anxious benefit from attending to rather than avoiding information about upcoming pain, such that high anxious individuals show better emotion outcomes when effortfully attending to pain (e.g., (Vervoort et al., 2014). If our findings are replicated in further studies, this may suggest that the function of attention control is different for adolescents with differing levels of anxiety. Additional analyses further attest to this notion. Specifically, we found that whilst increasing attention control was associated with better pain-related

outcomes in highly anxious adolescents (i.e., anticipating less pain and tolerating pain for longer), it was associated with poorer outcomes in lowly anxious adolescents (i.e., anticipating more pain and tolerating pain for less time). These findings may have implications for interventions that attempt to change pain attending (e.g., Attention Bias Modification, see (M. Dehghani et al., 2004)) or more general attention control capacities (e.g., Working Memory Training, see (Owens, Koster, & Derakshan, 2013)) for adolescents with persistent pain or pain-related anxiety.

Interestingly, we found that catastrophizing about pain, unlike anxiety, did not interact with attention control to impact adolescents' selective attending to pain. Catastrophizing did, however, interact with attention control to influence attending to all faces. Specifically, there was a cross-over interaction so that for adolescents reporting high levels of attention control, higher catastrophizing was associated with increasing dwell time on *all* faces. Conversely, for adolescents reporting low levels of attention control, higher catastrophizing was associated with decreasing dwell time on *all* faces. Nonetheless, catastrophizing did not impact selective attending to pain faces. This is somewhat in contrast with our previous findings presented in Chapter Two (Heathcote et al., 2015), wherein catastrophizing did interact with attention control to predict adolescents' pain attending in a dot-probe task. This inconsistency may be due to the current study's methodological advances, for example using eye-tracking and personally relevant pain cues. Importantly, adolescents' attending to pain facial expressions that inform about an upcoming painful experience may well differ from their attending to pain faces which are not relevant to or useful for their own experience of pain (Van Damme et al., 2010). Discrepancies may also be due to differences in sample ages and therefore cognitive capacities, with the current study including younger participants. Indeed, it has recently been questioned whether younger children experience truly catastrophizing thoughts,

and it has instead been proposed that more general worry and anxiety is more relevant for younger children's pain outcomes (Eccleston et al., 2012).

This study has limitations. First, due to technical limitations of the eye-tracker, we excluded 17 participants, resulting in a small final sample size. The small final sample also precluded analyses of age effects, which may play a role in adolescent processing of pain. Second, eye-tracking does not measure covert attentional capture preceding saccades. Indeed, initial attention capture by threatening stimuli may occur covertly, prior to initial fixation (Armstrong & Olatunji, 2012). Third, we recognize that this is a single experimental observation and replication is needed, in particular by other laboratories.

Despite these limitations, this study adds to the limited number of studies currently available on youth attention and pain in three ways. 1) This is the first study to use eye-tracking within the context of adolescent pain, thereby overcoming issues of using manual reaction times to infer attention, and allowing us to discriminate in real time between initial attention capture and dwelling on pain cues in youth. 2) This is one of few studies to use ecologically valid and personally salient stimuli, wherein photographs of pain facial expressions provided adolescents with information about an upcoming personal pain experience (see also (Vervoort, Trost, & Van Ryckeghem, 2013)). 3) This is the first study to examine the role of effortful attention control in understanding both pain attending and theoretically and clinically meaningful outcomes. Based on our findings, we believe three areas would be fruitful for further research. First, as discussed in Chapter Two, whilst the Attention Control Scale (ACS) assesses an individual's general capacity to focus in the face of distraction and to shift attention, these capacities may differ from the ability to control attention in pain-specific contexts. In particular, anxious individuals may exhibit more difficulties controlling attention in pain than non-pain contexts. The fact that we found a

significant moderation effect of general attention control attests to the importance of this general capacity in influencing pain-specific constructs, however, examining attention control within the context of pain may further our understanding of this effect. Second, whilst the ACS has shown good utility in predicting attentional performance in experimental tasks (Derryberry & Reed, 2002), it will be important for future studies to also include other measures of attention control such as flanker tasks (that are reliant on behavioural responses and reaction times, e.g., (Eriksen & Eriksen, 1974; Fan et al., 2002)) as well as antisaccade tasks (that are reliant on eye-movement patterns, e.g., (Rommelse, Van der Stigchel, & Sergeant, 2008)). These measures may be particularly important in child and adolescent samples, as brain regions engaged in goal-directed attention are still changing during this period (Cohen Kadosh et al., 2014; Monk et al., 2003; C. A. Nelson et al., 2002; Spear, 2000b), and so attention control may be more challenging to self-report. Third, the extent to which the reported pattern of attending is clinically relevant will rely on a demonstration of these effects in clinical samples, and a demonstration that they are malleable under instruction, practice, or therapy (to be considered in Chapter Four).

The current findings extend our understanding of the role of adolescent anxiety in attending to pain cues, and anticipation and tolerance of pain. Our findings suggest that attention control is an important moderating factor for multiple outcomes relevant to young people's pain experiences.

Chapter 4

4

Attention Bias Modification Training for Adolescents with Chronic Pain: A Randomized Placebo-Controlled Trial

We report here a randomized placebo-controlled trial of Attention Bias Modification (ABM) in a clinical sample of youth with chronic pain. Adolescents with chronic pain (N = 66) were randomly assigned to complete eight bi-weekly sessions of dot-probe ABM or placebo training, or to a waitlist control group. We examined the relative effects of ABM on attention bias, pain symptomatology, pain catastrophizing, anxiety and depression symptoms, and disability. We also examined the relative effects of ABM on attention control, and whether attention control moderated ABM efficacy. We did not find evidence that ABM affected pain or pain-related outcomes compared with placebo training or no training. ABM also did not change attention bias or attention control in comparison with placebo training or no training, and baseline levels of attention control did not moderate ABM efficacy. Our findings suggest that dot-probe ABM training may not be efficacious for improving outcomes in young people with chronic pain. Given recent theoretical models suggesting that attention biases are driven by biased interpretations of pain and pain-related information, tools that target interpretation biases may be more useful for investigating the causal role of cognitive processes in paediatric pain going forward.

4.1. INTRODUCTION

Attention is central to many psychological models of chronic pain (Eccleston & Crombez, 1999, 2007; Pincus & Morley, 2001; Todd et al., 2015; Vlaeyen & Linton, 2000). In particular, an attention bias toward pain – the habitual selection of pain-related information over non-pain information – is argued to increase the salience of pain, enhance fear and catastrophizing, motivate avoidance of painful activities, and thus drive disability. Three meta-analyses have provided evidence that adult chronic pain patients demonstrate an attention bias towards pain-related stimuli, although findings are mixed and effect sizes are small (Crombez et al., 2013; Roelofs et al., 2002; Schoth et al., 2012). Studies in adult populations have also supported associations between pain-related attention biases and emotional factors such as pain-related fear, anxiety, and catastrophizing (Asmundson, Carleton, & Ekong, 2005; Asmundson & Hadjistavropoulos, 2007; Carleton, Asmundson, Collimore, & Ellwanger, 2006; He, Yu, Jiang, Wang, & Luo, 2014; Peters, Vlaeyen, & Kunnen, 2002).

Fewer studies have investigated attention bias in youth samples (J. E. Beck et al., 2011; Boyer et al., 2006; Hermann, Zohsel, Hohmeister, & Flor, 2008), a period when chronic pain may first emerge (Perquin et al., 2000). However, as in adult populations, there is some evidence for pain-related attention biases in youth with chronic pain (J. E. Beck et al., 2011; Boyer et al., 2006; van der Veek et al., 2014) and we recently provided evidence for associations between attention biases and emotional factors such as anxiety (Chapter Three; (Heathcote, Lau, et al., 2016)) and pain catastrophizing (Chapter Two; (Heathcote et al., 2015)). Following these cross-sectional investigations, studies are now employing higher quality designs to investigate the causal nature of attention bias in chronic pain. Whilst there are some prospective studies (see (Todd et al., 2015) for a review), intervention and training

studies are important for identifying mechanisms underlying causal links between attention bias, pain, and pain-related outcomes.

One promising tool is Attention Bias Modification (ABM), which was developed to study the role of attention bias in anxiety disorders. In ABM, the dot-probe paradigm that is most commonly used to measure attention bias has been adapted to implicitly train participants' attention towards or away from threat-related stimuli. Typically, ABM training away from threat-related stimuli is compared to a waitlist condition, and/or to a condition where participants are trained towards threat-related stimuli, or to a placebo training condition in which the standard dot-probe task (with no training contingencies) is used. To date, a number of studies to date have shown that ABM training *away* from threatening stimuli is superior to a waitlist control, training towards threat, or placebo training, in alleviating anxious symptoms in adults (Bar-Haim, 2010; Hakamata et al., 2010) and in young people (Eldar et al., 2012; Shechner et al., 2014).

Within the context of pain, six studies (in five papers) have examined the utility of ABM for reducing pain and improving pain-relevant outcomes in adults (Carleton et al., 2011; McGowan et al., 2009; Sharpe et al., 2012, 2015; Todd et al., 2016). Two of these studies employed ABM in chronic pain samples (Carleton et al., 2011; Sharpe et al., 2012), one in a sample of patients with acute pain (Sharpe et al., 2012), and three in university student samples (McGowan et al., 2009; Sharpe et al., 2015; Todd et al., 2016). In the student samples, ABM has generated robust effects on experimentally-induced pain, particularly on pain threshold. For example, McGowan and colleagues (McGowan et al., 2009) and Sharpe and colleagues (Sharpe et al., 2015) revealed that participants trained *away* from pain-related words, relative to training *towards* pain-related words, had a higher pain threshold in a cold pressor test (CPT).

Compared to studies using experimentally-induced pain, findings for ABM training in clinical samples with pain are more mixed. The three studies published to date have all compared ABM training away from pain words to placebo training. The single study with acute (back) pain patients (Sharpe et al., 2012) demonstrated that participants receiving ABM training reported significantly less average and current pain, and experienced pain for fewer days relative to those receiving placebo training. For the chronic pain samples, McGowan and colleagues (McGowan et al., 2009) found that participants receiving ABM training reported a relative improvement in current pain severity, although this finding did not reach significance with one-tailed analysis (p = .06). Sharpe and colleagues (Sharpe et al., 2012) reported no effects of ABM training on chronic pain patients' current pain severity. Interestingly, both studies with chronic pain samples measured only participants' current levels of pain at the time of testing, whereas average pain intensity and pain duration over the previous days or week may better capture clinically-meaningful pain-attention interactions in everyday life. However, these studies (McGowan et al., 2009; Sharpe et al., 2012) found relative improvements of ABM training on self-reported anxiety sensitivity, and Sharpe and colleagues (Sharpe et al., 2012) also found relative improvements of ABM training on self-reported functional disability. These findings suggest that ABM training away from pain-related stimuli, compared to placebo training, may lead to improvements in pain-related outcomes even without impacting the pain experience itself.

Taken together, there is preliminary evidence that attention bias may play a causal role in pain and pain-related outcomes, although findings across experimental, acute, and chronic pain samples are somewhat mixed. No studies have yet examined the utility of ABM within a paediatric pain sample. Studies in adolescent populations may be particularly important given the developmental importance of mastery over attention in adolescence (Cohen Kadosh et al., 2014; Monk et al., 2003), and the neurodevelopment of brain regions engaged in goal-

directed attention during this life period (Monk et al., 2003; C. A. Nelson et al., 2002; Spear, 2000b), thus precluding extrapolation from adult ABM data. Moreover, investigating the plasticity of pain-related attention during adolescence may allow consideration of its role in the early emergence and maintenance of chronic pain. Thus, the current study was designed to examine the utility of ABM training for adolescents with chronic pain.

Previous studies on attention bias in adult pain samples, as described above, offer suggestion of the most efficacious parameters for our training protocol. In particular, pain-related biases appear to be strongest when tasks use sensory pain stimuli (Crombez et al., 2013; Schoth et al., 2012), and ABM training effects also appear most consistent when training away from sensory as opposed to affective pain stimuli (McGowan et al., 2009; Sharpe et al., 2012, 2015). Also relevant, Dear and colleagues (Dear, Sharpe, Nicholas, & Refshauge, 2011a) revealed that pain-related attention biases are strongest when using stimuli that are idiosyncratically selected to be personally relevant to each participant, indicating that personalized stimuli may also be most efficacious in ABM training. Within the psychopathology literature, there is evidence that training effects are greater when participants complete multiple sessions (Hakamata et al., 2010). Also relevant for our study design is current debate on the mechanism of change in ABM training. Whilst some models suggest that ABM targets valence-specific attentional selectivity, others propose that ABM targets top-down attention control, driven by the recruitment of the dorsolateral prefrontal cortex (Browning, Holmes, Murphy, Goodwin, & Harmer, 2010; Heeren, De Raedt, Koster, & Philippot, 2013). This debate is particularly relevant for the application of ABM in youth samples, given the neuro-development of brain regions engaged in goal-directed attention at this stage (Monk et al., 2003; C. A. Nelson et al., 2002; Spear, 2000b). Indeed, in two studies with adolescent community samples (Chapters Two and Three), we found that the associations between adolescents' emotional response to pain and attention bias to pain, as

well as pain outcomes, were moderated by attention control (Heathcote et al., 2015; Heathcote, Lau, et al., 2016). Given these findings, we aimed to examine whether ABM would change attention control, and whether it would be differentially efficacious depending on participants' baseline levels of attention control.

Here we report a three-arm randomized controlled trial of ABM in adolescents with chronic pain, comparing ABM training to placebo training and to a waitlist control. We investigated the potential utility of multi-session ABM for reducing pain symptoms (primary outcome variable) in these young patients relative to the control conditions, as well as for reducing pain-related outcomes such as pain catastrophizing, emotional functioning, and disability (secondary outcome variables). We predicted that participants in the ABM condition would report less pain intensity over the previous week, and would experience pain for less time each day during the previous week, than adolescents in the placebo training or waitlist conditions. We also expected that ABM would improve pain-related outcomes such as pain catastrophizing, emotional functioning (anxiety and depression symptoms), and disability, relative to placebo training and waitlist conditions. In addition, we hypothesized that ABM would result in a significant reduction in attentional biases towards pain, and this reduction would not be observed in the placebo training or waitlist groups; and that changes in attention bias would be associated with better outcomes. Finally, we examined whether ABM would change levels of self-reported and experimentally-measured attention control, and whether ABM efficacy would be moderated by participants' baseline levels of attention control.

4.2. METHODS

This study was registered on the NIHR Clinical Research Network Portfolio in August 2014 (UK Clinical Trials Gateway: CPMS 17251).

Participants

Adolescents aged 10-18 years, with chronic non-cancer pain, were recruited from the Oxford Centre for Children and Young People in Pain (OxCYPP), part of the Nuffield Orthopaedic Centre at the Oxford University Hospitals. OxCYPP is part of an orthopaedic musculoskeletal referral system, receiving referrals from gastroenterology, neurology, orthopaedics, spinal units, rheumatology, and primary care physicians. Patients were eligible for the current study if they reported recurrent or persistent pain for more than three months. Patients were excluded if they had current severe mental health issues based on expert clinician judgment by a paediatric consultant clinical psychologist, or did not understand English. Participants were only eligible to take part in the study if they were not scheduled to receive multidisciplinary inpatient treatment during the intervention (training) phase. The recruitment period was between October 2014 and April 2016, and the final assessment session for the last participant took place in August 2016. Participants were recruited primarily for the current study investigating ABM training, but we also collected measures of interpretation bias at baseline (data reported in a later chapter). Patients and a parent/guardian were first approached about the study either following their first assessment session at the clinic, or following their second visit to the clinic during which they attended a pain education class with a small group of other patients and families. During these sessions, patients and their families were approached by a paediatric rheumatologist or the team's consultant clinical psychologist and asked if they would like to learn more about taking part in a research study. A member of the research team subsequently provided the families who were happy to be approached with an information sheet, answered questions about the study, and scheduled appointments. Seventy-three patients were interested in the study, and 67 agreed to take part. Reasons for not participating in the study were not recorded for patients who were approached but declined to take part. A CONSORT diagram illustrating the flow of

participants through each stage of the trial is shown in Figure 1. The first patient was recruited as a pilot participant and only completed a small number of measures to examine feasibility of testing in the hospital setting, and so the data from this participant were excluded from analyses. Thus, 66 patients were enrolled in the full study (55 female; *M* = 13.97 years; *SD* = 2.13). All patients were enrolled by the study's principle investigator (LCH). The National Research Ethics Service (NRES) approved this study.

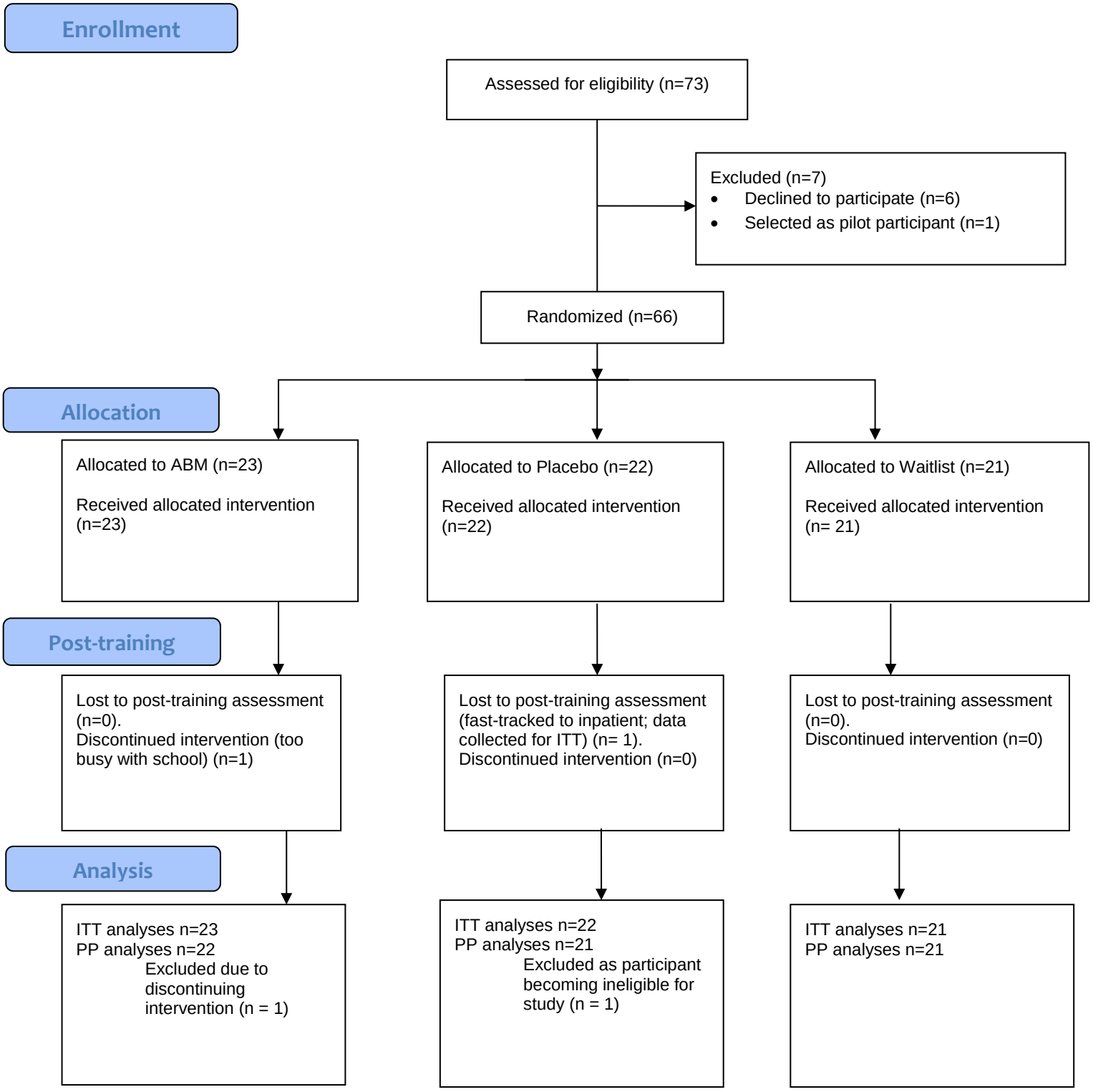
Procedures

Recruitment and assessment sessions took place at the Nuffield Orthopaedic Centre. At the baseline assessment session, parents/guardians first provided informed consent for their children. In addition, participants aged 16 or over provided informed consent for themselves. Participants younger than 16 years provided informed assent. Randomization took place following consent.

Randomisation

Eligible participants were randomly assigned to one of the three treatment arms (ABM, placebo, or waitlist), with an equal allocation ratio, based upon a computerized random number generator (www.random.org/). The principle investigator (LCH) performed randomisation. Randomisation was conducted immediately after participants and parents had consented to the study.

Figure 4.1. CONSORT Diagram Illustrating the Flow of Participants through the Study



Blinding

Participants assigned to ABM or placebo training were blinded to their treatment condition throughout the trial. Given that participants assigned to the waitlist condition were told that they would not receive the training games until after the final assessment session, it was not possible to blind participants assigned to this condition. Study physicians involved in the patients' otherwise normal care were blind to allocation. Only the principal investigator (LCH), who conducted all assessment sessions, was aware of the participants' treatment conditions, out of necessity for sending participants the correct training protocol.

Training Protocols

Participants in the ABM and placebo training groups were asked to complete eight training sessions, twice per week over four weeks. Participants were encouraged to do the training during normal waking hours, and to allow at least one day between the sessions. SMS reminders were sent to participants, parents, or both depending on the family's preference. Participants in the waitlist group did not complete any training between the baseline and post-training assessment, but were given the opportunity to complete the training after the final assessment session.

Assessment Sessions

At the baseline assessment session we collected demographic information and clinical history. At all assessment sessions (baseline and post-training) participants completed the measure of pain symptoms (primary outcome), followed by the dot-probe task, the flanker task, the physical tests, and finally the questionnaire measures. At the baseline assessment session participants also completed the Adolescent Interpretations of Bodily Threat (AIBT) task (data reported in Chapter Six). The post-training assessment was completed after the last

training session. In addition to the measures described above, participants completed two additional questions at the post-training assessment to provide subjective feedback on the training. Participants were compensated with an Amazon voucher after each assessment session (vouchers worth £100 in total), and travel expenses were reimbursed to parents. All adverse events, regardless of whether they were study-related, were monitored throughout and reviewed at each study assessment.

ABM and Placebo Training

ABM and placebo training were delivered using modified versions of the dot-probe task. During ABM and placebo training, stimuli were presented against a black background. Each trial began with a 500ms presentation of a white fixation cross in the middle of the screen. Participants were instructed to fixate their gaze on this location. Then, one stimulus pair comprising a pain-related stimulus and a neutral stimulus appeared and remained visible for 500ms. One stimulus was presented above and one below the fixation cross, with the distance from the stimuli to the centre of the screen as one-fourth the height of the screen. Immediately after the offset of these two stimuli, a letter 'p' or 'q' would appear in place of one of the stimuli (the probe). During ABM training, the probe *always* appeared in the previous location of the neutral stimulus, and stimulus pairs were randomly presented in each of the two possible combinations (probe up/pain stimulus down; probe down/pain stimulus up). Hence the ABM training implicitly directed participants to attend *away from* pain-related stimuli. During placebo training, the probe appeared equally often in the location of the pain-related stimulus and the neutral stimulus (as in the normal test version of the dot-probe task), and thus stimulus pairs were randomly presented in each of the four possible combinations (probe up/pain stimulus up; probe up/ pain stimulus down; probe down/ pain stimulus down; probe down/ pain stimulus up). In both training conditions, participants had to indicate

whether the probe was a ‘p’ or a ‘q’ by pressing the corresponding button on the (QWERTY) keyboard as quickly as possible. The ‘q’ key was pressed with the left index finger and the ‘p’ key was pressed with the right index finger. A new trial started after each response, or automatically when 2500ms elapsed without response. When a participant responded erroneously, the term ‘error’ briefly appeared on the screen (200ms). In order to ensure that participants maintained gaze at the middle of the screen, a number of digit trials were presented (see e.g., (Heathcote et al., 2015; Van Ryckeghem et al., 2012)). In these trials, the fixation cross was followed by a random digit between 1 and 9 for a duration of 100ms. Participants were instructed to type the number on the keyboard. The inter-trial interval was 1000ms after stimulus-pair trials, or 1100ms after digit trials. In the context of the current study, *congruent* trials were those where the probe was presented at the same location as the pain stimulus. *Incongruent* trials were those where the probe was presented at the same location as the neutral stimulus. Each training session consisted of 210 training trials (96 congruent trials, 96 incongruent trials, 18 digit trials), taking 12 minutes for participants to complete. Stimuli were presented in a randomized order across trials and participants, and trials were intermixed and randomly presented in two blocks, with a break between block one and block two.

The dot-probe tasks were programmed and presented using the INQUISIT Millisecond software package (INQUISIT 4.0). INQUISIT measures response times (RTs) with millisecond accuracy (Inquisit 4.0; Millisecond Software, Seattle, WA, USA). Participants completed all ABM and placebo training at home, using the INQUISIT Web interface. This interface allows participants to access each training task using a unique webpage address. The INQUISIT programme is downloaded to the participant’s local computer using a plugin. When the participant has finished the task, a data-file with the participant’s accuracy and response time scores is sent securely to the experimenter’s

INQUISIT account, allowing the experimenter to verify that the participant has completed each training task, and to monitor the participant's performance.

Measures

All primary and secondary outcome measures were completed at baseline and at the post-training assessment. The primary outcome was pain symptoms. Secondary outcomes included physical disability (indexed by a self-report and two physical tasks), pain catastrophizing, and generalised anxiety and depressive symptoms. We also measured attention bias and attention control at both assessments to examine whether training changed different aspects of attention and whether baseline levels of attention control moderated training efficacy. Details of training tasks and assessment measures are given below.

Demographics

At baseline, participants reported on demographic information including gender, age, ethnicity, school status, and number of siblings. Participants also reported on the onset of their pain (sudden or gradual), time since pain onset (months), and body locations where they experience pain.

Primary Outcome: Pain Symptoms

To assess pain symptoms, participants completed two 11-point visual analogue scales indicating their average pain intensity in the last week, and their pain intensity at the body part they experienced most problems with in the last week (hereafter referred to as 'most problematic pain') (0 = no pain; 10 = worst pain possible), as well as one 4-point visual analogue scale indicating the average duration of their pain each day in the last week (1 = less

than one hour; 4 = all day). These items were taken from the Brief Pain Inventory (Cleeland & Ryan, 1994).

Secondary Outcomes

Physical Disability

Participants' physical disability was assessed with one self-report measure and two physical tasks.

First, the Functional Disability Inventory (FDI) assesses perceived difficulty in performing common activities in the domains of school, home, recreation, and social interactions. Participants rate the difficulty they had in carrying out each activity in the preceding two weeks (0 = no trouble; 4 = impossible). The FDI consists of 15 items and yields a total score that can range from 0 to 60, with higher scores indicating greater disability. The FDI has yielded good reliability and validity for children and adolescents (Walker & Greene, 1991) and for youth with chronic pain (Kashikar-Zuck et al., 2011). Cronbach's alpha for our sample was .90 at baseline.

Second, two objective assessments of physical function were conducted. First, participants completed the Sit-to-Stand task, which comprised participants attempting to move from a seated to a standing position as many times as possible within 30 seconds. Second, participants completed the Cardio Wall task (http://embeddedfitness.nl/en/exergames/cardio-wall-2/), an interactive task in which participants are required to tap (using their hands) lights on a wall for 30 seconds. Participants must reach high and bend down low to tap the lights, and the maximum height can be adjusted according to the height of the participant.

Pain Catastrophizing

The Pain Catastrophizing Scale for children (PCS-C) was used to assess participants' catastrophic thinking about pain (Crombez et al., 2003). Pain catastrophizing is comprised of rumination, magnification, and helplessness. Participants rated 13 items on a 0-4 scale to create a total score from 0 to 52. Higher scores indicate more pain catastrophizing. The PCS-C has good reliability and validity for children above 9 years (Crombez et al., 2003). Cronbach's alpha for our sample was .88 for the total score at baseline.

Generalised Anxiety and Depression

Generalised anxious and depressive symptomatology was assessed using the Revised Child Anxiety and Depression Scale (RCADS) (Chorpita et al., 2000). The RCADS consists of 47 items which are scored on a 4-point Likert scale from never to always. Higher scores indicate increased symptoms of anxiety and depression. The RCADS comprises six subscales but here we only calculated scores for Generalized Anxiety Disorder (GAD) and Major Depressive Disorder (MDD) as we were interested in whether ABM training would improve general anxious and depressive symptomatology, and not symptoms specific to other anxiety disorders such as separation anxiety or social anxiety. The RCADS has yielded good reliability and validity for children and adolescents (Chorpita, Moffitt, & Gray, 2005; Esbjørn, Sømhovd, Turnstedt, & Reinholdt-Dunne, 2012; Mathyssek et al., 2013). Cronbach's alpha in this study was .86 for the GAD subscale and .86 for the MDD subscale at baseline.

Attention Bias Measurement (dot-probe) Task

To measure attention bias at baseline and post-training, we used a standard dot-probe task. The dot-probe task used to measure attention bias was similar to the placebo training

tasks (described above), in which participants were presented with stimulus pairs comprising one pain-related and one neutral stimulus, and were required to identify a probe (a letter 'p' or 'q'). Like in the placebo training, the pain-related stimuli, as well as the probe, were presented equally often at the top or bottom position of the screen in four possible combinations: pain stimulus top/probe top; pain stimulus top/probe bottom; pain stimulus bottom/probe bottom; pain stimulus bottom/probe top. Thus, the probe was equally likely to replace either a pain-related stimulus or neutral stimulus. Stimuli were presented in randomized order across trials and participants. Trials were intermixed and randomly presented in two blocks, with a break between block one and block two. However, unlike the training tasks, each measurement task also began with 20 practice trials comprising 16 neutral stimulus-pairs, none of which appeared in the experimental trials, as well as four digit trials. Thus, in total, each test phase (baseline and post-training) comprised 274 trials (96 congruent trials, 96 incongruent trials, 64 neutral-neutral trials, 18 digit trials), taking 12 minutes for participants to complete. Neutral-neutral trials were included as filler trials to reduce possible habituation to pain-related stimuli that might occur if all trials contained pain-related information. Participants completed all attention bias measurement tasks at the hospital, using the INQUISIT Lab programme on an experimenter-provided computer.

Attention Control Measures

Participants' levels of attention control were assessed with one self-report measure and one experimental measure.

The Attention Control Scale (ACS) (Derryberry & Reed, 2002) is a self-report questionnaire that comprises 20 items, and yields a total score that can range from 20 to 80, with higher scores indicating good attention control. The ACS has two subscale scores for attention focusing and attention shifting. The ACS has shown good reliability and predictive

utility, predicting resistance to interference in Stroop-like spatial conflict tasks as well as attentional disengagement from threat stimuli among highly anxious people (Derryberry & Reed, 2002). Furthermore, Matthews and colleagues (Mathews et al., 2004) showed greater activation in brain areas related to top-down regulation of emotion (i.e., rACC) in those reporting greater attention control. Attention control has also been measured with good reliability and validity in children (Muris et al., 2004). Cronbach's alpha in our sample was .81 for the total score at baseline.

The Fish Flanker Task (Christ, Kester, Bodner, & Miles, 2011; Rueda et al., 2004) is an experimental measure of attention control developed by Christ and colleagues (Christ et al., 2011). For this task, participants completed a series of computerized trials in which they saw a horizontal row of five fish. On each trial, participants were asked to respond as quickly as possible as to whether the centre fish was facing to the left or right (using the corresponding arrow keys on the computer keyboard). Response times were measured. Two trial types were administered: congruent and incongruent. On congruent trials, all five fish in the stimulus array pointed in the same direction. On incongruent trials, the four distracting fish pointed in the opposite direction of the central target fish. For each trial, stimuli were presented until a response was made or until more than 3000ms elapsed. After an inter-trial interval of 1500ms, a new trial was presented. If participants failed to respond within 3000ms, a tone and a message stating "Too slow" were presented. If participants pressed the incorrect arrow button, a tone and a message stating "Wrong response" were presented. Participants completed 120 experimental trials (60 congruent and 60 incongruent trials) that were randomly intermixed. Presentation was balanced such that all possible stimulus-flanker pairings were equally likely to occur. At intervals of 40 trials, children were offered a timed 30 second break. Response times on congruent and incongruent trials comprised outcome variables for this task.

Subjective Feedback on Training

At the post-training assessment, participants completed two six-point visual analogue scales (0 = Not at all; 5 = A lot) to gauge their enjoyment in completing the training ('How much did you enjoy doing the training?') and the degree to which participants think the training helped them ('How much do you think the training helped you?').

Materials

Dot-Probe (attention bias) Training and Measurement Stimuli

Three sets of picture stimuli, and one set of word stimuli, were used in the dot-probe assessment and ABM training tasks. Only picture stimuli were used at the assessment phases, whereas a mixture of picture and word stimuli were used for training.

Stimulus Set One was used at the baseline assessment session and for one of the training sessions. Stimulus Set Two was used at the post-training assessment session, but not during the training. Thus, attention biases were examined at the post-training assessment for non-trained stimuli. Both stimulus sets comprised 20 facial image stimuli each, presenting 10 child faces each (five male and five female). Stimuli were 160 x 264 pixels in size. All pictures were drawn from video clips of children taking part in a cold pressor pain experiment at the University of Ghent. Using these 40 pictures, 20 study slides were created. Each slide comprised two pictures of the same child. In eight of the slides, the child presented a neutral face in both pictures. These slides were used as practice trials. In the remaining 12 slides, there was one picture with the child presenting a neutral face and one picture with the child presenting a pain face. As these child stimuli were not previously validated, we asked participants at the post-training assessment session to rate each child face for pain intensity using a 0-10 Numeric Rating Scale (NRS) (i.e., 'How much pain has the child displayed on

the picture; anchors; 'no pain at all'; 'a lot of pain') (see Appendix A for results confirming that stimuli were attributed correctly).

Stimulus Set Three was used only for one of the training sessions. It comprised 12 facial image stimuli, presenting six adult faces (three male and three female). Stimuli were 160 x 264 pixels in size. All pictures were drawn from one-second video clips of simulated facial expressions of pain. These pictures were taken from a larger collection of stimuli, previously created and validated in the laboratory by Simon and colleagues (Simon et al., 2008). For these stimuli actors were videotaped while producing neutral facial displays and simulated facial expressions of different pain intensities. Using these 12 pictures, six study slides were generated. Each slide consisted of two pictures of the same adult, presenting a neutral face or a moderate pain face. These stimuli have been used in prior research examining attention bias to pain (see (Vervoort et al., 2012)). The validity of this stimulus set used is supported by previous findings of significantly different observer pain ratings between neutral and moderate pain facial expressions (see (Vervoort, Trost, & Van Ryckeghem, 2013)).

Stimulus Set Four was used for two of the training sessions. The total stimulus set comprised 54 pain/neutral word pairs which were matched for length and frequency (see Appendix B for fill list of words). However, only 12 word pairs were selected for each participant. These pairs were selected in order to best match the quality of pain experienced by each individual participant. Therefore, word stimuli were idiosyncratically matched for each participant. To select the 12 word pairs for each participant, participants were provided with the list of 54 pain-related words at baseline, and were asked to indicate how well each word described his/her pain (VAS: 0=Not at all; 5=Perfectly). Based on these ratings, we first selected words with the highest ratings (i.e., 5 out of 5). Next, we selected words with successively lower ratings until a total of 12 word-pairs were selected. If more than 12 words

were possible to select (i.e., with the highest ratings), we selected the words with the shortest length.

Statistical Analysis Plan

Missing Data

Per-protocol (PP) and Intention-to-treat (ITT) analyses were conducted. Following guidance from the Committee for Proprietary Medicinal Products (CPMP), the ITT analysis is considered primary and the PP analysis is considered supportive (Gupta, 2011) (PP analysis is presented in Appendix C). Regarding ITT analyses, for those enrolled participants who became ineligible for the study according to the protocol, but for whom we were still able to collect data, we included assessment data (post-training $N = 1$; participant was fast-tracked to an inpatient programme). For those participants whom we lost contact with or informed us of their withdrawal from the study, we used the last observation carried forward (LOCF) method (post-training $N = 1$; participant reported being too busy with schooling to complete training).

In addition, for those participants in attendance at each session, any questionnaires in which participants did not complete at least 75% of items are removed for that participant. Mean imputation using the relevant subscale for the individual participant's score is used for questionnaire items where less than 25% of the scale is missing.

Sample Size Determination

Given that there are no similar published studies on ABM in youth with chronic pain, nor on ABM in adults with chronic pain that compare three groups (i.e., ABM, placebo, and waitlist), formal sample size calculations were not considered reliable. However, a sample size of $n = 20$ in each group was determined on the basis that 1) this exceeds the sample size

determined by Sharpe and colleagues (Sharpe et al., 2012) for their study of ABM in adults with chronic pain, for which power analyses revealed a sample size of 12 participants per group was necessary to achieve 82% power with a significance level of 0.05 an effect size of 0.79 (based on findings from (MacLeod, Soong, Rutherford, & Campbell, 2007)), 2) this exceeds the sample size determined by Eldar and colleagues (Eldar et al., 2012) in youth with anxiety disorders (n = 10-15 in each group), and 3) Simmons and colleagues (Simmons, Nelson, & Simonsohn, 2011) suggest a minimum of n = 20 in each group to reduce the likelihood of false-positive findings.

Analyses

All analyses were conducted using SPSS 23.0 software. We first performed a series of one-way ANOVAs and chi-square tests to determine whether there were any differences between the three randomised groups (ABM, placebo, waitlist) on demographic variables, outcome variables, and task measures at baseline. Next, we performed *t*-tests to determine if participants demonstrated a significant attention bias towards pain at baseline, followed by a 2 (Congruency: congruent, incongruent) x 2 (Time: baseline, post-treatment) x 3 (Group: ABM, placebo, waitlist) ANOVA to establish whether there was a training effect. The main analyses comprised a series of 2 (time: baseline, post-training) x 3 (group: ABM, placebo, waitlist) ANOVAs for outcome variables. If analyses yielded any significant interaction effects which, when decomposed, revealed a significant effect of ABM training compared to placebo or waitlist, mediation analyses were performed to determine if change in attention bias mediated the change in the outcome variable. Additional 2 (Time: baseline, post-treatment) x 3 (Group: ABM, placebo, waitlist) ANOVAs were performed for attention control scores (ACS and flanker indices) to examine whether training impacted attention control. Finally, to determine whether participants' baseline levels of attention control

moderated training efficacy, all analyses for primary outcome variables were re-run including the centred attention control scores (ACS and flanker indices) as covariates.

Of note, due to technical difficulties with INQUISIT, dot-probe (attention bias) data were unavailable for one participant at baseline. Data from this participant were retained in all other analyses.

4.3. RESULTS

Participant Characteristics

Participant characteristics are presented in Table 4.1. Time since pain onset varied between 5 and 170 months (*M* = 45.7 months, *Mdn* = 35.5 months). Most participants reported multiple pains, with the most common pain problems including joint pain (*N* = 36, 54.5%), pain in legs or feet (*N* = 35, 53%), back pain (*N* = 33, 50%), and pain in hands or arms (*N* = 30, 45.5%). Twelve participants (18.2%) reported pain all over their body. When asked to indicate the body location where participants experienced the most pain, they most often indicated their back (*N* = 16, 24.2%), legs or feet (*N* = 15, 22.7%), or joints (*N* = 10, 15.2%). Participants reported an average pain intensity in the last three months of 6.55 out of 10 (*SD* = 1.63) and moderate levels of disability (as indexed by clinical reference points for the Functional Disability Inventory (FDI), *M* = 22.79, *SD* = 10.74, (Kashikar-Zuck et al., 2011)). Forty-four participants (66.7%) reported experiencing pain every day in the last three months, 20 (30.3%) reported pain on most days, and two (3%) reported pain on about one day per week. Thirty-one (47%) participants reported that they had taken pain medication at some point in the weeks leading up to the study. Randomization resulted in a balanced distribution across both conditions at baseline, with no significant group differences on all demographic, outcome, and task assessment measures (see Tables 4.1 & 4.2). As only one participant dropped out of the study before completing the training, we were unable to

examine whether there were any significant baseline differences between that participant and those participants who completed training. However, visual inspection of mean scores indicates that the participant who dropped out was similar across task and outcome measures.

Table 4.1. *Baseline demographic and pain characteristics*

Measure	ABM (n=23)	Placebo (n=22)	Waitlist (n=21)	Total (n=66)
Demographics				
Sex (F)	20 (87.0%)	17 (77.3%)	18 (85.7%)	55 (83.3%)
Age, y	13.48 (2.15)	13.95 (2.04)	14.52 (2.18)	13.97 (2.13)
Ethnicity (Caucasian)	21 (91.3%)	21 (95.5%)	19 (90.5%)	61 (92.4%)
Birth Country (UK)	21 (91.3%)	21 (95.5%)	20 (95.2%)	62 (93.9%)
Siblings (Yes)	21 (91.3%)	20 (90.9%)	18 (85.7%)	59 (89.4%)
Pain variables				
Time since pain onset (months)	44.70 (34.58)	39.18 (23.66)	53.48 (45.25)	45.65 (35.35)
School status (full time)	19 (82.6%)	18 (81.8%)	14 (66.7%)	51 (77.3%)
Pain onset (gradual)	13 (56.5%)	10 (45.5%)	16 (76.2%)	39 (59.1%)
Pain in more than one area (Yes)	21 (91.3%)	20 (90.9%)	17 (81.0%)	58 (87.9)
Pain at most problematic site (last week)	7.48 (1.83)	6.86 (1.64)	7.52 (1.63)	7.29 (1.71)
Average pain (last week)	6.09 (1.86)	6.18 (1.89)	6.33 (2.06)	6.20 (1.91)
Pain duration (last week)	3.17 (0.94)	3.39 (0.87)	3.67 (0.66)	3.39 (0.87)

Categorical variables: *N* (%); Ordinal/continuous variables: *Mean* (*SD*)
Nb. No significant differences between groups on any measures

Treatment Adherence

Out of the 45 participants who commenced either ABM or placebo training, 25 participants (55.6%) completed all eight training sessions as scheduled. Of the remaining participants, all participants completed five or more training sessions with the exception of one participant who dropped out before completing any training sessions (participant excluded from PP analyses).

Adverse Events

No adverse events reported by participants were study-related. No participants reported adverse events immediately following the baseline session. Eight participants reported adverse events at the post-training assessment. These included flu (N = 1), death of a grandparent (N = 1), visits to hospital emergency departments (N = 1), accident-related injury (N = 1), parent in accident (N = 1), minor medical procedures (N = 1), difficulties at school (N = 1), and death of a pet (N = 1). Four of these participants also reported pain or other physical symptoms as an adverse event; however, these were reported as unrelated to the study procedures. There were no significant differences in the number of adverse events reported between groups.

Data Preparation

Dot-Probe Task Data Preparation

Digit trials were first discarded. Consistent with previous research (Caes et al., 2011; Heathcote et al., 2015; Van Ryckeghem et al., 2012; Vervoort, Trost, & Van Ryckeghem, 2013), trials with errors, and responses shorter than 200ms or longer than 2000ms were also discarded. Within the present sample, the number of errors made by participants ranged from 2-30 (M = 11.06) for the baseline assessment, and from 1-73 (M = 11.63) for the post-training

assessment. After discarding these error trials, 0.2% of response times (RTs) in the remaining dataset at baseline, and 0.4% of RTs in the remaining dataset at post-training fell outside the range of 200ms to 2000ms. Probe detection latencies that were three SDs above or below the individual mean RT of correct responses for each trial type were also considered outliers and thus excluded from analyses (Caes et al., 2011; Heathcote et al., 2015; Koster et al., 2004; Vervoort, Trost, & Van Ryckeghem, 2013). This was the case for 1.4% of the RTs in the remaining dataset at baseline, and 1.6% of the RTs in the remaining dataset at post-training. Filler (neutral/neutral trials) were also discarded before means and SDs were calculated.

Fish Flanker Task Data Preparation

Consistent with previous research (Christ et al., 2011), trials with errors, and responses shorter than 200ms or longer than 3000ms, were discarded. Within the present sample, 2% of trials were removed from the baseline assessment, and 2.3% of trials were removed from the post-training assessment. As for the dot-probe data preparation, RTs that were three SDs above or below the individual mean RT of correct responses for each trial type were also considered outliers and thus excluded from analyses. This was the case for 1.7% of the RTs on congruent trials and 1.7% of the RTs on incongruent trials in the remaining dataset at baseline, and 1.8% of the RTs on congruent trials and 1.8% of the RTs on incongruent trials in the remaining dataset at the post-training assessment.

Intention to Treat Analyses

Attention Bias Analyses

Attention Bias at Baseline

There were no significant differences between reaction times to congruent or incongruent trials at baseline (t (64) = 0.33, p = .74), and the calculated bias score was not

significantly different from zero at baseline (t (64) = -0.33, p = .74), indicating no attentional biases to pain-related stimuli across the whole sample (see Table 4.2 for means and SDs).

Change in Attention Bias Following Training

A 2 (Congruency: congruent, incongruent) x 2 (Time: baseline, post-treatment) x 3 (Group: ABM, placebo, waitlist) ANOVA was conducted for dot-probe scores to assess whether a reliable training effect of ABM could be determined (see Table 4.2 for all means and SDs). Analyses revealed a main effect for time (F (1, 62) = 92.25, p < .001, η_p^2 = .60), indicating that all participants, regardless of training, had faster RTs at the post-training assessment compared to the baseline assessment (but collapsed across congruency) (See Table 3 for means, collapsed across groups). There were no main effects of congruency (F (1, 62) = 2.71, p = .11, η_p^2 = .04), or group (F (1, 62) = 1.06, p = .35, η_p^2 = .03), nor were there two-way interactions for time x group (F (2, 62) = 2.15, p = .13, η_p^2 = .07), congruency x group (F (2, 62) = 0.02, p =.98, η_p^2 = .001), or time x congruency (F (1, 62) = 1.50, p = .23, η_p^2 = .02). There was also no three-way interaction for time x congruency x group (F (2, 62) = 0.50, p =.61, η_p^2 = .02). Thus, the predicted training effect was not observed.

Table 4.2. *Means and SDs of outcome and process measures for each group at each time point (ITT analyses)*

Measure	ABM (n=23)		Placebo (n=22)		Waitlist (n=21)	
	Baseline	Post-training	Baseline	Post-training	Baseline	Post-training
Primary outcomes						
Pain at most problematic site (last week)	7.48 (1.83)	7.17 (1.85)	6.86 (1.64)	6.95 (1.59)	7.52 (1.63)	7.05 (2.01)
Average pain (last week)	6.09 (1.86)	6.57 (1.67)	6.18 (1.89)	5.91 (0.43)	6.33 (2.06)	6.24 (2.00)
Pain duration (last week)	3.17 (0.94)	2.91 (1.04)	3.39 (0.87)	3.14 (1.04)	3.67 (0.66)	3.48 (0.19)
Secondary outcomes						
FDI	22.14 (10.70)	19.35 (10.01)	23.90 (12.29)	19.73 (13.31)	22.69 (9.64)	19.64 (9.89)
PCS-C	28.87 (10.96)	26.52 (10.05)	30.41 (10.30)	24.91 (11.77)	24.95 (8.44)	20.76 (10.63)
RCADS-Depression	12.17 (6.40)	11.52 (6.49)	12.73 (6.28)	12.09 (7.07)	10.24 (5.12)	9.81 (5.91)
RCADS-Generalised anxiety	7.97 (4.34)	6.65 (3.96)	7.36 (4.14)	6.32 (3.88)	5.38 (4.01)	5.86 (3.82)
ACS	47.13 (8.22)	50.26 (8.93)	47.82 (9.14)	48.14 (9.50)	49.55 (8.42)	50.57 (10.93)
Sit-to-stand task	12.57 (3.73)	13.13 (3.92)	14.77 (4.56)	14.77 (5.01)	13.90 (4.10)	15.48 (3.74)
Cardio wall task	45.26 (11.60)	49.70 (13.79)	48.36 (14.08)	52.91 (16.24)	49.43(16.11)	56.10 (13.41)
Dot-probe task						
Congruent trials (RT)	651.54 (125.25)	564.01 (141.62)	630.89 (124.35)	537.65 (92.77)	659.62 (112.32)[a]	625.28 (125.14)
Incongruent trials (RT)	651.19 (129.62)	557.37 (128.63)	627.00 (127.31)	534.35 (97.37)	661.38 (114.08)[a]	617.17 (120.39)
Attention bias index (RT)	-0.36 (20.93)	-6.64 (27.23)	-3.89 (23.09)	-3.30 (21.88)	1.76 (23.37)[a]	-8.12 (16.81)
Fish Flanker task						
Congruent trials (RT)	544.67 (81.64)	571.66 (139.08)	531.13 (131.74)	501.69 (129.29)	553.47 (123.27)	552.06 (107.12)
Incongruent trials (RT)	588.61 (90.93)	612.65 (147.01)	551.77 (122.45)	545.66 (140.33)	602.05 (161.94)	601.40 (119.24)

FDI = Functional Disability Index; PCS-C = Pain Catastrophizing Scale - Child; ACS = Attention Control Scale; RCADS = Revised Child Anxiety and Depression Scale.

[a]*N* = 20

Nb. One-way ANOVAs indicate no significant differences between groups on any measures at baseline or post-training (all p > .05)

Primary Outcome Measures

A series of 2 (Time: baseline, post-treatment) x 3 (Group: ABM, placebo, waitlist) ANOVAs were conducted on pain symptoms. There was a significant main effect of time for pain duration (F (1, 63) = 4.88, p = .03, η_p^2 = .07), indicating that all participants, regardless of training, experienced pain for less time each day (See Table 4.3 for means and SDs, collapsed across groups). There were no main effects for average pain or most problematic pain, and contrary to our hypotheses, there were no interaction effects (see Table 4.4 for ANOVA results of all measures).

Secondary Outcome Measures

A series of 2 (Time: baseline, post-training) x 3 (Group: ABM, placebo, waitlist) ANOVAs were conducted on secondary outcome measures. There were main effects of time for functional disability (F (1, 63) = 18.44, p < .001, η_p^2 = .23), pain catastrophizing (F (1, 63) = 20.00, p < .001, η_p^2 = .24), generalised anxiety (F (1, 63) = 6.71, p = .01, η_p^2 = .10), sit-to-stand task (F (1, 63) = 6.91, p = .01, η_p^2 = .10), and cardio wall task (F (1, 63) = 18.67, p < .001, η_p^2 = .23), indicating that participants improved over time on these measures, regardless of training group (See Table 4.3 for means and SDs, collapsed across groups). The only significant group x time interaction effect was for generalised anxiety (F (2, 63) = 5.19, p = .01, η_p^2 = .14). Bonferroni-corrected analyses of simple main effects revealed that there was a significant decrease in generalised anxiety from baseline to post-training assessment in the ABM group (p = .002) and the placebo group (p = .02), but not the waitlist group (p = .27) (see Table 4.2 for means and SDs). No other interaction effects reached significance (see Table 4.4 for ANOVA results of all measures).

Table 4.3. *Means and SDs of outcome and task measures at each time point, collapsed across groups (ITT analysis)*

Measure	Baseline	Post-training
Primary outcomes		
Pain at most problematic site (last week)	7.29 (1.71)	7.06 (1.80)
Average pain (last week)	6.20 (1.91)	6.24 (1.89)
Pain duration (last week)	3.39 (0.87)	3.17 (1.00)
Secondary outcomes		
FDI	22.91 (10.80)	19.57 (11.01)
PCS-C	28.14 (10.10)	24.15 (10.94)
RCADS-Depression	11.74 (5.98)	11.16 (6.49)
RCADS-Generalised anxiety	6.94 (4.25)	6.29 (3.85)
ACS	48.11 (8.53)	49.65 (9.70)
Sit-to-stand task	13.73 (4.18)	14.42 (4.31)
Cardio wall task	47.62 (13.88)	52.80 (14.55)
Dot-probe task		
Congruent trials (RT)	647.04 (119.82)[a]	574.72 (125.37)
Incongruent trials (RT)	646.14 (123.15)[a]	568.72 (119.69)
Attention bias index	-0.90 (22.20)[a]	-6.00 (22.28)
Fish flanker task		
Congruent trials (RT)	542.96 (112.35)	542.10 (127.95)
Incongruent trials (RT)	580.61 (127.14)	586.74 (137.59)

FDI = Functional Disability Index; PCS-C = Pain Catastrophizing Scale - Child; ACS = Attention Control Scale; RCADS = Revised Child Anxiety and Depression Scale.
[a] $N = 65$

Table 4.4. *ANOVA results for all outcome measures, comparing baseline to post-training assessments (ITT analysis)*

Measure	Effect	*df*	*F*	*p*	η_p^2
Primary outcomes					
Pain at most problematic site	Time	1,63	1.11	.30	.02
	Group	2,63	0.50	.61	.02
	Time x Group	2,63	0.58	.56	.02
Average pain (last week)	Time	1,63	0.04	.84	.001
	Group	2,63	0.16	.85	.01
	Time x Group	2,63	1.69	.19	.05
Pain duration (last week)	Time	1,63	4.88	**.03**	.07
	Group	2,63	2.24	.12	.07
	Time x Group	2,63	0.04	.96	.001
Secondary outcomes					
FDI	Time	1,63	18.44	**.00**	.23
	Group	2,63	0.06	.94	.002
	Time x Group	2,63	0.30	.74	.01
PCS-C	Time	1,63	20.00	**.00**	.24
	Group	2,63	1.74	.18	.05
	Time x Group	2,63	1.07	.35	.03
RCADS-Depression	Time	1,63	2.46	.12	.04
	Group	2,63	0.90	.41	.03
	Time x Group	2,63	0.04	.96	.001
RCADS-Generalised anxiety	Time	1,63	6.71	**.01**	.10
	Group	2,63	1.08	.35	.03
	Time x Group	2,63	5.19	**.01**	.14
Sit-to-stand task	Time	1,63	6.91	**.01**	.10
	Group	2,63	1.62	.21	.05
	Time x Group	2,63	2.81	.07	.08
Cardio wall task	Time	1,63	18.67	**.00**	.23
	Group	2,63	0.87	.42	.03
	Time x Group	2,63	0.35	.70	.01
Dot-probe task					
Attention bias index	Time	1,62	92.25	**.00**	.60
	Group	2,62	1.06	.35	.03
	Congruency	1,62	2.71	.11	.04
	Time x Group	2,62	2.15	.13	.07
	Congruency x Group	2,62	0.02	.98	.001
	Time x Congruency	1,62	1.50	.23	.02
	Time x Congruency x Group	2,62	0.50	.61	.02
Attention control					
ACS	Time	1,62	4.04	**.049**	.06
	Group	2,62	0.37	.70	.01
	Time x Group	2,62	1.11	.34	.04
Fish flanker task	Time	1,63	0.04	.85	.001
	Group	2,63	1.16	.32	.04

Congruency	1,63	153.05	**.00**	.71
Time x Group	2,63	1.17	.32	.04
Congruency x Group	2,63	2.08	.13	.06
Time x Congruency	1,63	1.54	.22	.02
Time x Congruency x Group	2,63	2.11	.13	.06

Figures in bold indicate significance ($p < .05$).

Attention Control Analyses

Change in Attention Control after Training

To examine whether ABM training changed self-reported attention control, we conducted a 2 (Time: baseline, post-training) x 3 (Group: ABM, placebo, waitlist) ANOVA with the Attention Control Scale (ACS) score as the outcome variable. There was a main effect of time (F (1, 62) = 4.04, p = .049, η_p^2 = .06) (See Table 4.3 for means and SDs, collapsed across groups), but no interaction effect (see Table 4.4 for ANOVA results of all measures), indicating that all participants reported increased attention control at the post-training assessment, regardless of group.

To examine whether ABM training changed experimentally-measured attention control, we conducted a 2 (Congruency: congruent, incongruent) x 2 (Time: baseline, post-treatment) x 3 (Group: ABM, placebo, waitlist) ANOVA for RTs on the flanker task. There was a main effect of congruency (F (1, 63) = 153.98, $p < .001$, η_p^2 = .71) (See Table 4.3 for means and SDs, collapsed across groups), indicating that participants were slower on incongruent than congruent trials. There were no other main effects, and no interactions effects (see Table 4.4 for ANOVA results of all measures).

Moderation of Training Effect by Attention Control

To examine whether baseline levels of self-reported attention control moderated training efficacy, we performed the same series of ANOVAs described above for primary outcome measures and dot-probe indices, but including the centred ACS score as a covariate. Analyses revealed a significant time x group x attention control interaction for most problematic pain intensity (F (2, 59) = 3.51, p = .04, η_p^2 = .11). To interpret this three-way interaction, we first performed three additional ANOVAs as described above, but separately for each group (ABM, placebo, waitlist). These additional analyses revealed a significant time x attention control interaction for the waitlist group (F (1, 18) = 8.88, p = .01, η_p^2 = .33), but not for the ABM (F (1, 21) = 0.54, p = .47, η_p^2 = .03) or placebo group (F (1, 20) = 0.05, p = .82, η_p^2 = .003). Thus, attention control was a significant moderator for the waitlist but not the ABM or placebo groups. To aid interpretation of the significant two-way interaction for the waitlist group, we computed a pain change score by subtracting participants' most problematic pain at post-training assessment from their most problematic pain at baseline. A bivariate correlation revealed that participants (in the waitlist group) with higher self-reported attention control at baseline reported significantly reduced pain at the post-training assessment (r = -.58, p = .01). There were no other significant three-way interactions for primary outcome measures, or for dot-probe indices, and the main effects of time for pain duration and dot-probe indices remained unchanged (data that remained unchanged are not reported again).

To examine whether baseline levels of experimentally-measured attention control moderated training efficacy, we again performed the same series of ANOVAs described above for primary outcome measures and dot-probe indices, but this time including a centred interference score as a covariate. This interference score was derived from the flanker task by

subtracting mean RTs on congruent from incongruent trials. Thus a higher interference score indicates lower attention control. There were no significant two- or three-way interaction effects for primary outcome measures or for dot-probe indices, and the main effect of time for pain duration and dot-probe indices remained unchanged (data that remained unchanged are not reported again).

Subjective Feedback

Participants who completed ABM or placebo training reported that they enjoyed completing the training to a moderate degree (M = 3.58, Range = 2-5), and that they believed the training helped them to a moderate degree (M = 2.66, Range = 0-5). When asked to predict whether they received ABM or placebo training, 29 participants (65.9%) thought that they had completed placebo training, and there was no significant difference between groups in predicted training received (ABM group: 16 (72.7% placebo); placebo group (13 (59.1% placebo); X^2 (1) = 0.91, p = .34).

4.4. DISUCSSION

This study presents a three arm randomized placebo-controlled trial of multi-session Attention Bias Modification (ABM) for adolescents with chronic pain. We were unable to reject the null hypotheses that there were no significant differences between ABM training and placebo training or no training (waitlist condition) on any primary or secondary outcome measures. There were significant improvements for a number of primary and secondary outcomes, however this may be explained by spontaneous remission or by practice effects, as all groups displayed similar gains. There was a significant reduction in generalized anxiety symptoms from baseline to the post-training assessment; however this was evident for both the ABM and placebo groups (but not waitlist). ABM training also did not significantly

impact attention control measures in comparison to placebo training and no training. We found that self-reported attention control moderated the effect of training group on participants' most problematic pain, however these effects were driven by changes in the waitlist group, indicating that attention control did not moderate training efficacy. Findings were similar across per-protocol and intention-to-treat analyses (see Appendix C for PP analyses), suggesting that we can be confident in our results and the conclusions drawn (Gupta, 2011). Although preliminary, we found that multi-session dot-probe ABM training did not reduce pain symptoms, physical disability, pain catastrophizing, or anxiety and depression for adolescents with chronic pain, as measured immediately post-treatment.

Our findings are somewhat inconsistent with previous findings in adult samples. Most relevant for comparison are the two studies that have investigated ABM in adults with chronic pain (Carleton et al., 2011; Sharpe et al., 2012). Unlike Carleton and colleagues (Carleton et al., 2011), we found no effects of ABM training on pain outcomes. In addition, Sharpe and colleagues (Sharpe et al., 2012) found that ABM training led to a significant improvement in disability, and both studies found improvements in a small number of pain-related emotional factors. We did not replicate these findings with our sample of children with chronic pain. A number of differences between the current and previous studies may explain inconsistencies. First, we used different measurement tools. Studies conducted in adult populations found training-related changes in measures of anxiety sensitivity and fear of pain, which we did not measure. It may be that ABM influences only these specific constructs. However, our previous findings in community samples suggest that biases are associated with catastrophizing and generalized anxiety (Chapters Two and Three; (Heathcote et al., 2015; Heathcote, Lau, et al., 2016)), indicating that these constructs are relevant for youth samples. In addition, whilst the adult studies measured only current pain, we asked participants to report on pain in the preceding week. However, both scales provide

relevant outcomes for these populations. In addition, whilst the adult patients reported current pain only, our young patients reported three pain outcomes (average pain, pain at most problematic body site, pain duration), arguably increasing sensitivity to detect changes in pain experiences. Second, participants in the current study completed all training sessions at home, whilst for the previous studies training was completed partially or entirely in the clinic. It has previously been argued that at-home ABM training may be negatively influenced by the participant being in comfortable and familiar surroundings, whereas a level of mild anxiety, for example by visiting the clinic, is necessary for activating and therefore changing threat-related biases (Carlbring et al., 2012).

Some findings were in line with other ABM studies for pain and psychopathology populations. First, there was no evidence of a pain-related attention bias at baseline in our sample, and no evidence that biases changed following training, thus replicating findings from Sharpe and colleagues (Sharpe et al., 2012). This may explain our null findings. Indeed, previous findings on ABM efficacy for anxiety and depressive disorders indicate that effects on outcomes are most consistently found when biases exist at baseline (e.g., (Fox, Zougkou, Ashwin, & Cahill, 2015)), and when training successfully changes biases (Clarke, Notebaert, & MacLeod, 2014). On the other hand, Sharpe and colleagues (Sharpe et al., 2012) demonstrated effects of ABM training on pain-related outcomes despite no change in bias. Similar findings are also evident in the psychopathology literature, where individuals appear to benefit from training despite no group bias being observed (Bar-Haim, 2010). Also relevant are findings that the dot-probe task does not demonstrate good reliability as a measurement tool in pain populations (Dear et al., 2011b), suggesting that changes in biases following ABM training, or a lack thereof, may not be a reliable indicator of actual changes in attentional functioning. In addition, despite promising findings for ABM in early studies on anxiety disorders, ours is also not the first to show null results of training on clinical

outcomes. For example, Carlbring and colleagues (Carlbring et al., 2012) also found that ABM training was not efficacious beyond placebo training for individuals with social anxiety. Given increasing interest in ABM as a treatment tool for chronic pain (Sharpe et al., 2012; Todd et al., 2015), and early attempts to patent and market ABM training as a treatment for anxiety disorders (Bernstein, 2013), our null findings provide important information for this field as it emerges.

Despite inconsistencies between the current and previous studies, our study design also had significant advances to previous studies on ABM in pain populations. First, word training stimuli were idiosyncratically selected to be personally relevant for each participant in this study, specifically to match the quality of his/her pain. Previous findings suggest that personal relevance of pain stimuli is important for eliciting biases (Dear et al., 2011a), therefore ABM training may be most efficacious when using such personalized stimuli. Second, we included two physical tasks (the sit-to-stand task and the cardio wall task) that provided objective measures of physical functioning. These tasks are frequently used in physiotherapy sessions to assess disability in chronic pain patients and therefore reflect measures that are used in clinical practice to make decisions about patients' treatment needs and progress.

Third, we considered the impact of ABM training on attention control, including both a self-report and an experimental measure. This is potentially important given recent debate on mediators of training effects, and suggestion that ABM may impact attention control rather than valence-specific attentional selectivity. Moreover, given our recent findings that attention control moderates the association between attention bias for pain and pain-related outcomes in adolescent community samples (Chapters Two and Three; (Heathcote et al., 2015; Heathcote, Lau, et al., 2016)), we also examined whether baseline levels of attention control would moderate training efficacy. Our findings did not indicate that ABM training

changed attention control, nor did attention control moderate training outcomes. We did find that attention control moderated participants' most problematic pain in the waitlist group, suggesting that attention control may be an important predictor of natural changes in pain outcomes over time. These findings warrant replication. Nonetheless, future studies may consider including measures that tap into different components of attention control. For example, the flanker task is generally considered a measure of interference, whilst good control of attention also comprises other factors including the ability to shift and focus attention. Future studies may consider using other tasks such as the Attention Network Test (that is designed to test alerting, orienting, and executive control) (Fan et al., 2002), as well as antisaccade tasks (that are reliant on eye-movement patterns and are designed to test inhibition) (Hutton & Ettinger, 2006). In addition, whilst the Attention Control Scale (ACS) assesses an individual's general capacity to focus in the face of distraction and to shift attention, these capacities may differ from the ability to control attention in pain-specific contexts. In particular, anxious adolescents with chronic pain may exhibit more difficulties controlling attention in pain than non-pain contexts. Examining attention control within the context of pain may be more relevant to current understanding.

In addition to contributing to current knowledge on the role of attention bias in pediatric pain, findings presented here add to our understanding of intervention delivery in this population. First, recruitment of patients into the study was very successful, and most patients who were approached by the team agreed to take part. Anecdotal evidence from the current study suggests that the computer-game interface was appealing to participants, suggesting that future interventions using a similar interface may achieve a similarly high recruitment success rate. Second, retention was high, and findings suggest that participants were engaged with the computer training. We were able to collect data remotely, which revealed high levels of accuracy and fast response times. Subjective feedback also indicated moderate levels of

task enjoyment and perceived usefulness. This information is particularly important given current concerns over the face validity of ABM training in adult samples (Beard, 2011). Given the need for novel interventions that are both cost-effective and easy-to-access, we provide evidence that computerized training may be a promising platform for delivering interventions to youth with chronic pain.

In conclusion, we report here the first trial of ABM in a clinical sample of youth with chronic pain. We did not find evidence that ABM affected pain or pain-related outcomes compared with placebo training or no training. ABM also did not change biases in comparison with placebo training or no training. Novel tools are needed that better shift biases in order to draw conclusions about the causal role of attention bias in child and adolescent pain. Nonetheless, our findings suggest that dot-probe ABM training may not be efficacious for improving outcomes in young people with chronic pain. Given recent theory suggesting that attention biases are driven by biased interpretations of pain and pain-related information (Crombez et al., 2015; Todd et al., 2015), tools that target interpretation biases may be more useful for investigating the role of cognitive biases in pain going forward. The next two chapters in this thesis will thus move to consider the role of pain-related interpretation biases in adolescent pain experiences.

Chapter 5

An edited version of this chapter has been published as follows:

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5

Negative Interpretation Bias and the Experience of Pain in Adolescents

Negative interpretation bias, the tendency to appraise ambiguous situations in a negative or threatening way, has been suggested to be important for the development of adult chronic pain. This is the first study to examine the role of a negative interpretation bias in adolescent pain. We first developed and piloted a novel task that measures the tendency for adolescents to interpret ambiguous situations as indicative of pain and bodily threat. Using this task in a separate community sample of adolescents (*N*=115), we then found that adolescents who catastrophize about pain, as well as those who reported more pain issues in the preceding three months, were more likely to endorse negative interpretations, and less likely to endorse benign interpretations, of ambiguous situations. This interpretation pattern was not, however, specific for situations regarding pain and bodily threat, but generalized across social situations as well. We also found that a negative interpretation bias, specifically in ambiguous situations that could indicate pain and bodily threat, mediated the association between pain catastrophizing and recent pain experiences. Findings may support one potential cognitive mechanism explaining why adolescents who catastrophize about pain often report more pain.

5.1. INTRODUCTION

Pain is commonly experienced in youth, but for some can become chronic and debilitating (King et al., 2011; Perquin et al., 2000). Guided by theoretical models (Crombez, Eccleston, Van Damme, Vlaeyen, & Karoly, 2012; Todd et al., 2015; Vlaeyen & Linton, 2000), adult research suggests that cognitive factors, such as the tendency to process ambiguous information as indicative of pain and bodily threat, can maintain and even play a causal role in the development of chronic pain (Keogh & Cochrane, 2002; Keogh et al., 2004; Khatibi et al., 2014; Vancleef et al., 2016, 2009; Vancleef & Peters, 2008). Indeed, a range of experimental tasks show that chronic pain patients interpret ambiguous information in more threatening ways compared with control subjects (Edwards & Pearce, 1994; Khatibi et al., 2015; McKellar et al., 2003; Pincus et al., 1994, 1996). Moreover, studies suggest that this interpretation bias acts as a cognitive mechanism underlying pain-related vulnerability, mediating the association between emotional responses to pain and pain outcomes (Keogh & Cochrane, 2002; Keogh et al., 2004; Vancleef et al., 2016).

In youth, research has also demonstrated that cognitive factors contribute to the experience of pain. For example, studies suggest that youth with chronic pain are characterised by biases in the way they attend to (J. E. Beck et al., 2011; Boyer et al., 2006; Hermann et al., 2008; van der Veek et al., 2014) and remember (Koutantji, Pearce, Oakley, & Feinmann, 1999) pain-related information. Moreover, recent research, including findings presented in Chapter Two, suggest that these attention and memory biases also characterise youth who catastrophize about the experience and potential consequences of pain (Asmundson et al., 2012; Heathcote et al., 2015; Noel, Rabbitts, Tai, & Palermo, 2015; Vervoort, Trost, & Van Ryckeghem, 2013), suggesting that biases may be relevant for pain-related vulnerability in youth (Noel, Palermo, Chambers, Taddio, & Hermann, 2015). Further, current theoretical models indicate that biases in attention, memory, and

interpretation interact with each other to impact pain chronicity (Crombez et al., 2015; Noel, Palermo, et al., 2015; Todd et al., 2015). However, unlike studies on attention and memory bias, there are currently no studies measuring interpretation biases in child and adolescent pain, despite the potential importance of this mechanism for the maintenance/development of chronic pain.

In this paper, we first aimed to develop a novel task that measures the tendency for adolescents to interpret ambiguous situations as indicative of pain and bodily threat. Although some previous adult studies have used words and facial expressions as ambiguous stimuli (Edwards & Pearce, 1994; Khatibi et al., 2014; Pincus et al., 1994, 1996), these often lack contextual information, raising questions about their ecological validity. In the field of anxiety and depression (Miers, Blöte, Bögels, & Westenberg, 2008; Stopa & Clark, 2000), and in a small number of innovative adult pain studies (Keogh & Cochrane, 2002; Keogh et al., 2004; Vancleef et al., 2009; Vancleef & Peters, 2008), alternative paradigms use vignettes to describe real-world situations where it is unclear what is happening. The individual is asked to imagine herself in the situation, and asked what she thinks is happening. She is then asked whether particular interpretations come to mind (interpretation generation) and how strongly she believes the interpretations to be true (interpretation belief). These interpretations may be negative, benign, or positive. These tasks can also probe the content-specificity of biases, that is, whether biases exist only for information specifically relating to the individual's disorder (e.g., chronic pain may be associated with biased interpretations of information only regarding pain and bodily threat) or extend to other domains of functioning (e.g., social situations).

Using this new vignette-based task, we then aimed to examine associations between negative interpretation biases, pain catastrophizing, and recent pain experiences in a community sample of adolescents. We hypothesized that adolescents who catastrophize about

pain would endorse more negative interpretations, and reject more benign interpretations of ambiguous situations. We also hypothesized that the same pattern of biased interpretations would be associated with reporting greater pain in the preceding three months, as indexed by a composite score of pain intensity, frequency, and interference. We explored whether these associations would be stronger for interpretation generation versus belief, and would be specific to situations regarding pain and bodily threat or would extend to social situations. Finally, we investigated whether a negative interpretation bias would mediate the relationship between pain catastrophizing and recent pain experiences (see Figure 5.1). That is, we test the hypothesis that the tendency to negatively interpret ambiguous information as indicating pain and bodily threat is one potential cognitive mechanism by which adolescents with high pain catastrophizing report greater pain experiences.

5.2. METHODS

Participants

One hundred and nineteen participants from 8 classes in two secondary schools in the South of England were invited to take part. All agreed. Parents provided informed consent for their children. Participants aged 16 or over provided informed consent for themselves while participants younger than 16 provided informed assent. All participants were fluent in English. Four participants were excluded from analysis as they did not complete at least 25% of items on one or more questionnaires (N = 2) or because their participant numbers did not match across the different measures (N = 2). The final sample entered in the analysis thus comprised 115 adolescents (58 female; *M* = 14.8 years; *SD* = 1.79, age range = 11-18 years). A power analysis based on effect sizes from similar studies conducted in adults (i.e. those which assessed correlations between pain catastrophizing measures and interpretation biases in community samples) found that 102 participants would be required to detect a correlation

of 0.27 at $p<0.05$ with 80% power, two-tailed. A correlation of 0.27 reflects the middle value of previously reported correlations that ranged from 0.17 to 0.45 (Olthuis, Stewart, Watt, Sabourin, & Keogh, 2012; Vancleef et al., 2016; Vancleef & Peters, 2008). For task development purposes (described under '*Measures'*), data was first collected from two additional adolescent samples to generate items that were truly ambiguous (defined as those that elicited most variability among adolescents in terms of selection of negative versus benign interpretations). The study was approved by the Central University Research Ethics Committee at the University of Oxford.

Measures

Adolescent Interpretations of Bodily Threat (AIBT) task

This task is a new, computerized measure of interpretation bias for adolescents. The task comprises eight vignettes describing ambiguous situations that may be interpreted as relating to bodily threat or pain, and eight vignettes describing ambiguous social situations. The situations reflect events that may occur at school, at home, or during everyday adolescent life. The task structure is based on the self-report instruments developed by Clark and colleagues (Clark et al., 1997) for adult populations and by Miers and colleagues (Miers et al., 2008) for adolescents, and on the lexical decision task developed by Vancleef and colleagues (Vancleef et al., 2009).

In the AIBT task, participants are first presented with one of the ambiguous situations in the centre of the screen. For example, *"Your dad jumps out of his chair and puts his hands to his face, making a loud noise. He is…."*. The situation is ambiguous because there are at least two different possible word endings, reflecting different interpretations. The participants are instructed to read the situation and to imagine themselves in the situation before pressing the spacebar. After pressing the spacebar, participants are offered one possible end word that

resolves the situation in a negative or benign manner. For example, *"Your dad jumps out of his chair and puts his hands to his face, making a loud noise. He is **hurt**"*. Participants then rate whether or not that interpretation popped into their mind on a scale of 1 to 5 (1 = did not pop into my mind, 3 = might pop into my mind, 5 = definitely pops into my mind). After rating the first word, they are presented with a second word that resolves the situation in a different way; for example, *"Your dad jumps out of his chair and puts his hands to his face, making a loud noise. He is **surprised**"*, and are again asked to rate if that interpretation popped into their mind. Finally, participants are asked to select the interpretation that most easily popped into their mind. After the participants have responded to all 16 scenarios, they receive new instructions. Participants are informed that they will see the same situations again, however this time, they are asked to rate their *belief* that each interpretation would actually be happening in that situation. The addition of this belief question has been used in a number of previous studies to measure interpretation bias in adults and children (e.g., (Clark et al., 1997; Miers et al., 2008)). All items and interpretations are presented in a fixed random order.

The ambiguous situations used in the AIBT task were selected on the basis of two pilot studies. Participants for these pilot studies (age 16-18 years) were also recruited from secondary schools in the South of England, and gave informed consent to participate. In pilot study one, 100 adolescents were presented with 45 ambiguous situations that could be interpreted as relating to **pain or bodily threat**. In pilot study two, 45 adolescents were presented with 32 **social** situations that could be interpreted benignly or negatively. Some of the pain/bodily situations were adapted from an interpretation bias task developed for Dutch adults by Vancleef, Peters, and De Jong (Vancleef et al., 2009) while some of the social items were adapted from a cognitive bias modification task for adolescents (Belli & Lau, 2014). All remaining situations were generated by the authors and assessed for age-relevance by a group

of adolescents taking part in work experience or research at the University of Oxford. Participants were presented with threatening and benign words for each ambiguous situation, and were asked to assign a likelihood percentage between 0 and 100 to each word, and to select the word that they thought was most likely to end the sentence. Following both pilot studies, the experimenters selected the most ambiguous items on the basis of four stages. First, we selected items for which, on average, 30-70% of participants had chosen the benign word to end the sentence. This removed items for which participants were very likely to choose the negative word (i.e., under 30% benign choice) or the benign word (i.e., over 70% benign choice). Second, we removed any items for which one of the words was given a likelihood percentage, on average, less than 30%. This removed items that contained any words that participants considered were very unlikely to end the sentence. Third, we removed any items that correlated with the other items below the 0.1 level (i.e., corrected item-total correlation in reliability analysis) on the ratings of benign words, ratings of negative words, or on forced choice. One final bodily threat item was removed on the basis that one of the possible end words might not be understood by younger participants, leaving eight social and eight bodily threat items. These 16 items were included in the final AIBT task (See Appendix D). The validity of the social items were investigated by assessing interpretations of these items and their correlation with social anxiety scores (Appendix E).

Pain Catastrophizing Scale for Children

This assessed adolescents' catastrophic thinking about pain (Crombez et al., 2003) and was adapted from the adult Pain Catastrophizing Scale (Michael J. L. Sullivan et al., 1995). It consists of 13 items that yield a total score from 0 to 52. Higher scores indicate more pain catastrophizing. Subscale scores for rumination, magnification, and helplessness

can be derived. The PCS-C has good reliability and validity for children above nine years (Crombez et al., 2003). Cronbach's alpha in this study was .90 for the total score.

Recent Pain Experiences

Four items from the Brief Pain Inventory (BPI) (Cleeland & Ryan, 1994) assessed subjective experiences of pain in the preceding 3 months.). The BPI has been widely used to measure pain experiences in non-clinical and clinical populations. Participants rated their average pain intensity and worst pain intensity in the last 3 months (0 = no pain; 10 = worst pain possible), the amount that pain had interfered with daily activities over the last 3 months (0 = I don't miss out on any activities; 10 = I miss out on all activities), and the frequency of their pain over the last 3 months (1 = on less than one day each month; 6 = every day). As in previous studies (McGrath, Latimer, Finley, & Chambers, 2009; Vervoort et al., 2006), the pain ratings were highly correlated (all r = .38 < > .65). To avoid performing multiple analyses, a summed score was created by across the four scales (which ranged from 1 to 36). Similar composite scores have been usefully applied in previous studies to measure pain experiences in healthy children and adolescents (Vervoort et al., 2006), adolescents with chronic pain (Keogh & Eccleston, 2006), adolescent cancer patients (Ameringer, 2010), adult cancer patients (Wardley et al., 2005), and aged populations (Parmelee, Katz, & Lawton, 1991).

Revised Child Anxiety and Depression Scale

To assess whether biases in interpretations were linked specifically to pain variables rather than to co-occurring generalized anxious or depressive symptomatology, we administered the Revised Child Anxiety and Depression Scale (RCADS (Chorpita et al., 2000)). The RCADS consists of 47 items, scored on a 4-point Likert scale from never to

always. Higher scores indicate more anxiety or depression. The RCADS comprises six subscales but in this study, we only calculated scores for Generalized Anxiety Disorder and Major Depressive Disorder. The RCADS has yielded good reliability and validity for children and adolescents (Chorpita et al., 2005; Esbjørn et al., 2012; Mathyssek et al., 2013). Cronbach's alpha in this study was .85 for the GAD subscale and .88 for the MDD subscale.

Social Anxiety Scale – Adolescent version

To establish the validity of our social items within the AIBT (see Appendix E), we investigated biases in relation to adolescent social anxiety symptoms as assessed using the 22-item Social Anxiety Scale – Adolescent version (SAS-A) (La Greca & Lopez, 1998). Each item is scored on a 5-point Likert scale from 1 (not at all), to 5 (all the time). As four items are filler items, total scores range from 18 to 90. The SAS-A has yielded good reliability and validity for adolescents (Garcia-Lopez et al., 2002; La Greca & Lopez, 1998; Storch, Masia-Warner, Dent, Roberti, & Fisher, 2004). Cronbach's alpha in this study was .92 for the total score.

Procedure

All testing sessions took place during school hours. After completing the consent/assent forms participants were seated in front of a computer at a distance of approximately 60cm from the screen, to complete the AIBT task. Participants completed two practice trials and the experimenter gave additional verbal instructions for any participants who were unclear (please contact the lead author for a full script). After finishing the interpretation bias task, participants completed the online questionnaires before being debriefed. The whole procedure took about one hour.

Data analysis plan

The AIBT task provides ratings of interpretations (i.e., participants' ratings of the different interpretations on a scale of 1-5) and forced choice of interpretation (i.e., participants' choice of one interpretation for each situation). As these different response formats were highly correlated within each condition (all r = .63 < > .83), and yielded similar results, only analysis on the ratings data is presented here. However, analysis and results for the forced choice data can be found in Appendix F.

To examine the effects of **pain catastrophizing** on negative and benign interpretations in bodily threat and social situations. We used a 2 x 2 x 2 multivariate repeated-measures ANCOVA design with valence (negative/benign words), context (bodily threat/social), and block (interpretation generation/belief), as within-subject factors, and pain catastrophizing score entered as a covariate. This approach was chosen because we were interested in whether the effects of pain catastrophizing on both negative and benign interpretations depended on whether participants reported on interpretations coming to mind (interpretation generation) or their belief in those interpretations being true (interpretation belief) (i.e., block), and whether interpretations varied across context (bodily threat/social situations). Performing a single analysis to investigate these questions afforded the most stringent approach to reduce error from multiple comparisons. Pain catastrophizing was entered as a covariate to retain the full range of scores on this continuous measure. To examine the effect of **recent pain experiences** on negative and benign interpretations in bodily threat and social situations, we used a similar multivariate repeated-measures ANCOVA as described above but with the pain composite score included as the covariate. If an association between a pain variable and interpretation bias became apparent, we examined whether this association was due to anxious or depressive symptomatology through partial correlations.

To examine whether interpretation bias mediated the association between pain catastrophizing and recent pain experiences (Figure 5.1), we used the PROCESS tool from Hayes (Hayes, 2013). The method first establishes whether or not the direct path (i.e., path *c* in Figure 5.1) is significant, then, examines whether the indirect effect (combined effects of path *a* and *b* in Figure 5.1) is significantly different from sero by producing a confidence interval for the indirect effect of the predictor variable (pain catastrophizing) on the outcome variable (recent pain experiences), through the mediating variable (interpretation bias), and which may not include zero. The Hayes (Hayes, 2013) method moves beyond the causal steps approach popularised by Baron and Kenny (Baron & Kenny, 1986) by minimizing the number of tests needed to examine mediation, increasing power to detect a possible effect, and enabling quantification of the indirect (mediating) effect (Hayes, 2013).

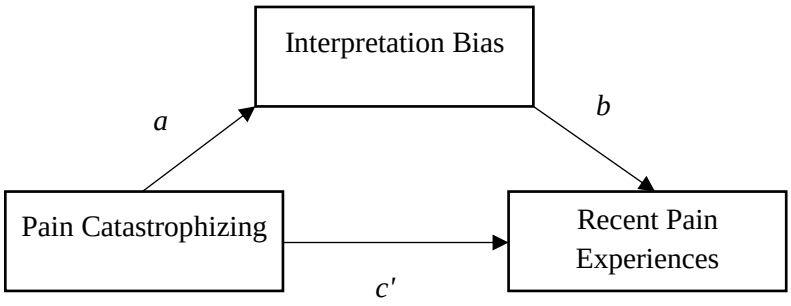


Figure 5.1. Proposed mediation model

For all analyses, $p < .05$ was the cut-off for statistical significance. For the ANCOVA analyses, Partial Eta Squared (partial η^2) effect sizes were reported (small effect size = 0.01; medium effect size = 0.06; large effect size = 0.14 (Cohen, 1988) (Olejnik & Algina, 2000)).. For t-test analyses, Cohen's D (*d*) effect sizes were reported (small effect size = 0.2; medium effect size = 0.5; large effect size = 0.8 (Cohen, 1988)). For mediation analyses, kappa-

squared (kappa^2) effect sizes were reported (small effect size = .01; medium effect size = .09; large effect size = .25 (Preacher & Kelley, 2011)).

5.3. RESULTS

Five participants reported experiencing no pain in the preceding three months, and were therefore told that they did not have to complete the remaining questions about their recent pain experiences. This was because an indication of 'no pain' meant that participants could only report the lowest possible options for all following questions about pain intensity, frequency, and interference. These participants were therefore assigned the lowest possible scores by the experimenter, so as to keep testing time to a minimum That is, they were assigned scores of zero for pain intensity and interference, and a score of one for frequency.

Participant characteristics

As can be seen in Table 5.1, participants reported low to moderate levels of pain catastrophizing. These levels are consistent with those reported previously in similar samples (Heathcote et al., 2015). In addition, participants reported low levels of generalized anxiety and depressive symptomatology, and moderate levels of social anxiety, which is again expected of an unselected sample, and in line with figures from similar samples (Alfano, Zakem, Costa, Taylor, & Weems, 2009; García-López, Olivares, Hidalgo, Beidel, & Turner, 2001). Participants also reported low to moderate levels of pain in the preceding three months, which is again expected of an unselected sample. Girls reported more symptoms of generalized anxiety ($t(113) = -2.54$, $p < .05$) and depression ($t(113) = -2.78$, $p < .01$) than boys. There were no significant sex differences in social anxiety ($t(113) = -1.71$, *ns*), pain catastrophizing ($t(113) = -0.52$, *ns*), or recent pain experiences ($t(113) = 1.16$, *ns*).

Table 5.1. *Means, SDs (in brackets), and Ranges (in italics) for pain indices and emotional symptomatology*

	Mean (SD)	*Possible Range (actual range)*
Generalized anxiety	8.01 (3.79)	*0-18 (1-18)*
Depression	10.00 (5.60)	*0-30 (0-30)*
Social anxiety	50.61 (13.80)	*18-90 (20-87)*
Pain catastrophizing	18.09 (8.97)	*0-52 (1-42)*
Pain frequency (last 3 months)	3.61 (1.41)	*1-6 (1-6)*
Average pain intensity (last 3 months)	3.02 (1.94)	*0-10 (0-8)*
Worst pain intensity (last 3 months)	5.63 (2.33)	*0-10 (0-10)*
Pain interference (last 3 months)	1.66 (2.11)	*0-10 (0-9)*
Recent pain experiences (composite)	13.92 (6.17)	*1-36 (1-27)*

Pain catastrophizing and interpretation bias

To examine the association between pain catastrophizing and interpretations, a 2 (valence) x 2 (block) x 2 (context) ANCOVA was conducted with pain catastrophizing score entered as a covariate (Table 5.2 presents the *M*s and *SD*s of this analysis). The multivariate test yielded significant effects for **valence**, $F(1, 113) = 31.61$, $p < .001$, partial $\eta^2 = .22$; **context**, $F(1, 113) = 42.45$, $p < .001$, partial $\eta^2 = .27$; and **block**, $F(1, 113) = 4.83$, $p < .05$, partial $\eta^2 = .04$. There was also a significant two-way interaction for **valence x block**, $F(1, 113) = 11.94$, $p = .001$, partial $\eta^2 = .10$, and a significant three-way interaction for **valence x block x context**, $F(1, 113), = 10.87$, $p = .001$, partial $\eta^2 = .09$. There was also a significant **valence x pain catastrophizing** interaction, $F(1, 113), = 14.86$, $p < .001$, partial $\eta^2 = .12$. Pain catastrophizing did not interact with context or block to form any three- or four-way interactions.

Descriptives for all main effects are presented in Table 5.3. To explore the valence x block x context interaction (which subsumed the valence x block interaction), we performed 2 (valence) x 2 (context) repeated-measures ANOVAs separately for each block. This revealed a significant valence x context two-way interaction in both blocks (interpretation generation: $F(1, 114)$, = 7.36, p <.01, partial η^2 = .06; interpretation belief: $F(1, 113)$, = 7.812, p <.01, partial η^2 = .06). To further decompose these interactions, we performed t-tests comparing negative and benign interpretations in bodily threat versus social situations for each block. These revealed that negative interpretations received significantly lower ratings than benign interpretations when participants considered their belief in those interpretations (Bodily threat: $t(114)$ = -8.73, p <.001, d = 0.815; Social: $t(114)$ = -4.56, p <.001, d = 0.43) but not when considering how easily interpretations came to mind (Bodily threat: $t(114)$ = 1.66, *ns, d = 0.16*; Social: $t(114)$ = -1.58, *ns, d = 0.15*).

To further examine the **valence x pain catastrophizing** interaction, we conducted Pearson correlations separately for adolescents' ratings of negative and benign interpretations, collapsed across block and context. These analyses revealed that adolescents with higher levels of pain catastrophizing were significantly more likely to endorse negative interpretations (r = .22, p < .05), and significantly more likely to reject benign interpretations (r = .33, p < .001), than adolescents with low levels of pain catastrophizing. After controlling for anxiety and depressive symptoms, the effect for benign ratings was still significant (r = .22, p < .05). However, the effect for negative ratings was no longer significant (r = .02, *ns*).

Table 5.2. *Means and SDs (in brackets) for the AIBT ratings data (rating scale possible range = 1-5)*

Interpretation generation (Block 1)	
Bodily threat negative word	3.38 (0.59)
Bodily threat benign word	3.25 (0.56)
Social negative word	2.93 (0.73)
Social benign word	3.11 (0.65)
Interpretation belief (Block 2)	
Bodily threat negative word	3.15 (0.57)
Bodily threat benign word	3.87 (0.53)
Social negative word	2.93 (0.62)
Social benign word	3.37 (0.59)

Table 5.3. *Means and SDs (in brackets) for main effects on AIBT task parameters (rating scale possible range = 1-5)*

Benign Interpretations	3.40 (0.43)
Negative Interpretations	3.10 (0.43)
Bodily Threat Interpretations	3.41 (0.29)
Social Interpretations	3.09 (0.30)
Interpretation Generation	3.17 (0.32)
Interpretation Belief	3.33 (0.28)

Pain experiences and interpretation bias

To examine the association between recent pain experiences and interpretations, a 2 (valence) x 2 (block) x 2 (context) ANCOVA was conducted with the recent pain experiences score entered as a covariate. The multivariate test yielded significant effects for **valence**, $F(1, 113) = 29.71$, $p < .001$, partial $\eta^2 = .21$; **context**, $F(1, 113) = 22.67$, $p < .001$, partial $\eta^2 = .17$; and **block**, $F(1, 113) = 17.24$, $p < .05$, partial $\eta^2 = .13$. There was also a significant two-way interaction for **valence x block**, $F(1, 113) = 14.69$, $p = .001$, partial $\eta^2 = .12$, and a significant

three-way interaction for **valence x block x context**, $F(1, 113), = 10.15$, $p = .01$, partial $\eta^2 = .08$. There was also a significant **valence x recent pain experiences** interaction, $F(1, 113), = 14.46$, $p < .001$, partial $\eta^2 = .11$ and a significant **block x recent pain experiences** interaction, $F(1, 113), = 3.94$, $p < .05$, partial $\eta^2 = .03$. As the main effects and interaction effects not including pain experiences were explored earlier, these were not explored again here.

To further examine the **valence x recent pain experiences** interaction, we conducted Pearson correlations separately for adolescents' ratings of negative and benign interpretations, collapsed across block and context. These analyses revealed that adolescents who recently experienced more pain were significantly more likely to endorse negative interpretations ($r = .33$, $p < .001$), and significantly more likely to reject benign interpretations ($r = -.21$, $p < .05$), than adolescents who experienced less pain. To further examine the **block x recent pain experiences** interaction, we conducted Pearson correlations separately for adolescents' ratings of interpretations coming to mind and their belief in those interpretations being true, collapsed across valence and context. Whilst there was a significant interaction effect, neither correlation when performed separately was significant (interpretation generation: $r = .17$, *ns*; interpretation belief: $r = -.0$, *ns*).

Testing for mediator effects

The analysis reported above confirmed that a negative interpretation bias was associated with both higher pain catastrophizing and higher experiences of recent pain. Analysis was therefore performed to determine whether a negative interpretation bias mediated the association between pain catastrophizing and recent pain experiences. To perform this analysis, we created an Interpretation Bias Score (IBS) by subtracting ratings for benign interpretations from ratings of negative interpretations. This score provides a single

measure of interpretation bias, with higher scores indicating more negative interpretations. Given that context (bodily threat/social) and block (interpretation generation/belief) did not interact with valence and pain catastrophizing or recent pain, we first performed the mediation analysis using an IBS that was collapsed across context and block. However, given that we may expect a more specific role of bodily threat interpretations to act as a mediator between two pain-related variables, we also performed the mediation analysis separately for the bodily threat items and the social items.

First, the analyses confirmed that pain catastrophizing is significantly associated with recent pain experiences (path *c* in Figure 5.1), $F(1, 113), = 25.02$, $p < .001$. Next, when using the IBS collapsed across context and block, there was a significant indirect effect of pain catastrophizing on recently experienced pain through interpretation bias, $b = 0.05$, BCa CI [0.015, 0.115]. This represents a small-to-medium effect, $kappa^2 = .077$, 95% BCa CI [0.026, 0.161]. Next, when using the IBS for bodily threat items only (collapsed across block), there was again a significant indirect effect of pain catastrophizing on recently experienced pain through interpretation bias, $b = 0.04$, BCa CI [0.009, 0.111]. This represents a small-to-medium effect, $kappa^2 = .066$, 95% BCa CI [0.014, 0.157]. Finally, when using the IBS for social items only (collapsed across block), the indirect effect was not significant, $b = 0.02$, BCa CI [-0.010, 0.076]. This indicates that, when considered separately, only a negative interpretation bias for ambiguous information regarding pain and bodily threat mediated the association between pain catastrophizing and recent pain experiences. A negative social interpretation bias did not play a mediating role.

5.4. DISCUSSION

In this study we developed a novel, computerized task (the AIBT task) that measures the tendency for adolescents to interpret ambiguous situations as indicative of pain and bodily

threat. Based on two pilot samples, we developed the final AIBT task. In a third and independent sample of adolescents, we then investigated whether negative bodily-threat interpretations were associated with pain catastrophizing and recent pain experiences. Critically, we also examined whether a negative interpretation bias mediated the association between pain catastrophizing and recent pain experiences. We found that adolescents who catastrophize about pain, and those who reported recent pain issues, endorsed more negative interpretations, and rejected more benign interpretations, of ambiguous situations, with a medium-to-large effect. This interpretation pattern was not, however, specific for situations regarding pain and bodily threat, but generalized across social situations as well. We also found that a negative interpretation bias, specifically in situations regarding bodily threat, mediated the association between pain catastrophizing and recent pain experiences. This finding may explain why adolescents who catastrophize about pain also report more pain.

This study extends current findings. Whilst previous studies on adolescent pain and cognitive bias, including previous chapters in this thesis, have focused on biased attending to pain cues (J. E. Beck et al., 2011; Boyer et al., 2006; Heathcote et al., 2015; Hermann et al., 2008; Vervoort, Trost, & Van Ryckeghem, 2013), this is the first study to consider biased interpretations of ambiguity in youth. We present here a novel tool for investigating pain-related interpretation bias using ecologically valid information. This tool allows us to measure whether adolescents endorse or reject both negative and benign interpretations of the same situations, as well as to differentiate interpretation generation (i.e., whether an interpretation comes to mind) from interpretation belief (i.e., belief that the interpretation is true). Investigating the nature of these interpretational processes in developmental samples is important for advancing theory. Current cognitive-affective models of pain indicate that biases in interpretation, attention, and memory do not exist in isolation, but instead, interact with each other to impact pain chronicity (Crombez et al., 2015; Todd et al., 2015).

Moreover, recent models posit that negative interpretations may in fact *drive* biased attending to pain (Crombez et al., 2015; Eccleston & Crombez, 1999; Todd et al., 2015; Vlaeyen & Linton, 2000). Thus, the current study provides a platform for examining the reciprocal relationships between different cognitive biases across an important developmental period, when pain often first becomes chronic (Perquin et al., 2000).

Our findings are in line with previous adult studies demonstrating an association between negative interpretations of ambiguous information and individual differences in pain-related vulnerability constructs (Khatibi et al., 2014; Vancleef et al., 2009; Vancleef & Peters, 2008). Our findings are also in line with adult studies demonstrating that the tendency to interpret ambiguous information as indicative of bodily threat plays a mediating role in the association between emotional response to pain and pain outcomes (Keogh & Cochrane, 2002; Keogh et al., 2004; Vancleef et al., 2016). In particular, our findings suggest that a negative interpretation bias may be one reason why individuals who have a high emotional response to pain are also more likely to experience and report more pain. Of note, though, as mediation analysis on cross-sectional data cannot establish the direction of relationships, our findings and previous findings from adult samples could also be interpreted in the opposite direction. For example, recent experiences of pain could lead to a negative interpretation bias as well as greater catastrophizing in response to pain, and causality remains to be established in future studies. Nonetheless, we also extend findings from adult samples. For example, our findings indicate that pain-related vulnerability may be associated with both the tendency to endorse negative interpretations as well as to reject benign interpretations of ambiguous situations. Also, when controlling for symptoms of generalized anxiety and depression, only the association with benign interpretations remained significant. This effect certainly remains to be replicated in adults, in other healthy child and adolescent samples, and in adolescent chronic pain samples. However, if we see a similar pattern in clinical and prospective studies,

this could suggest that biased interpretations are a target for treatment, and moreover, rather than necessarily reducing negative interpretations, interventions that encourage more benign interpretations could be more potent at specifically reducing pain-related vulnerability.

It is interesting that we did not always find evidence for a specific effect of bodily threat interpretations as separate from negative social interpretations. While adult data have not directly addressed this issue, data do largely support a more general bias (Keogh & Cochrane, 2002). In our sample of adolescents, those who catastrophized about pain, and those who experienced more recent pain issues, showed a more general bias that extended across both bodily threat as well as social situations. This may be because pain catastrophizing and acute pain are indeed associated with a more general tendency to interpret all ambiguous situations in a negative way, and thus with an information processing system that is broadly biased in favour of negative material (Keogh & Cochrane, 2002). On the other hand, our effects may be specific to bodily threat and social situations, but may not extend beyond these two domains. Indeed, adolescence is a time of increased independence from parents, increased focus on peer interactions, and thus increased salience of social situations. It may be important for future studies measuring individual differences in cognitions associated with pain experiences or chronic pain to consider situations outside of the social and bodily threat domains, for example situations relating to academic performance or attainments.

Despite this, we did find (in post-hoc analysis) that negative interpretations specifically regarding bodily threat, but not social threat, mediated the association between pain catastrophizing and recent pain experiences. This indicates some degree of specificity in the association between biased interpretations and pain-specific measures, and warrants continued investigation of these relationships, rather than moving to a model of shared vulnerability across pain and psychopathology. It will also be interesting to examine whether there is more specificity in adolescent chronic pain samples, when the young person has been

in pain for many months or years, and when issues regarding pain and bodily threat are more relevant for their concerns. Of further note, the valence-specific effects reported above also did not differ for interpretation generation compared with interpretation belief. We did find that, independent of valance, pain experiences interacted with block, but with a very small effect size. Indeed, when performing separate analyses, neither correlation reached significance, suggesting that there is not a large difference in the associations between pain experiences and interpretation generation versus interpretation belief. However, we may expect that interpretation generation and interpretation belief would play different roles in prospective or clinical populations, and we therefore suggest retaining both blocks in the AIBT task for future studies.

This study has limitations, some that we can address in future research. First, all measures were self-report, and shared method variance could inflate the chance of finding significant effects. Incorporating measures of more automatic, reflexive processing (e.g., lexical decision tasks (Vancleef et al., 2009), incidental learning tasks (Khatibi et al., 2014), or word priming tasks (Vancleef et al., 2016)) within the context of ambiguous situations, particularly within youth samples, would be useful and revealing. Second, not all adolescents who catastrophize about pain develop chronic pain. Relatedly, we measured prior pain experiences rather than prospective pain-related outcomes. The presence and clinical relevance of a negative interpretation bias within an adolescent patient sample remains to be established (see Chapter Six). In addition, longitudinal studies will be necessary for assessing whether a negative interpretation bias predicts the transition from acute to chronic pain or whether, as noted above, a negative interpretation bias is merely the outcome of increased acute pain. Training studies can also be useful for illuminating causality. There already exist novel cognitive training tools that use simple learning mechanisms to encourage more negative or benign interpretations of ambiguous situations (Lau, 2013; MacLeod, 2012; Salemink & Wiers,

2012). If training a more negative interpretation bias can increase pain catastrophizing and acute pain, and likewise, if training a more benign bias can reduce these, this could provide evidence that a negative interpretation bias plays a causal role in the pain experience.

In addition, it will be important to consider why and how an adolescent might develop a negative interpretation bias. Recent findings from the psychopathology literature provide some suggestions, demonstrating that biased interpretations of ambiguous information can be transferred from parents to children (Julie a. Hadwin, Garner, & Perez-Olivas, 2006; Lester, Seal, Nightingale, & Field, 2010). Future studies investigating family influence on young people's interpretations of ambiguous situations within the context of pain will be highly informative. Furthermore, it will be important to examine whether our findings extend to younger child samples. Recent findings from the psychopathology literature suggest that interpretation biases are acquired in later childhood, only once certain cognitive and social building blocks are in place (Field & Lester, 2010). These findings are relevant not only for guiding future studies of interpretation bias in child pain, but also for adapting the AIBT task. In particular, there may be developmental differences in younger and older children's ability to understand the difference between interpretation generation and belief. It will therefore be important to examine the utility of our task for investigating biases in younger samples.

The current findings extend our understanding of the role and nature of cognition in adolescent pain. Using a novel computerized task, we demonstrated that cognitive biases toward threat, particularly in the interpretation of ambiguous information, might play an important role in adolescent pain experiences. Critically, we provided preliminary evidence that a tendency to interpret ambiguous situations as indicative of pain and bodily threat may be a cognitive mechanism that connects pain catastrophizing with actual pain experiences. The AIBT task could now usefully be employed in clinical and longitudinal samples to

understand how interpretation bias, in reciprocal relations with other cognitive biases and emotional responses to pain, contribute to acute and chronic pain in adolescents.

Chapter 6

An edited version of this chapter is currently under review as follows:

Heathcote, L. C., Jacobs, K., Eccleston, C., Fox, E., & Lau, J. Y. F. (under review). Biased Interpretations of Ambiguous Bodily Threat Information in Adolescents with Chronic Pain.

6

Biased Interpretations of Ambiguous Bodily Threat Information in Adolescents with Chronic Pain

Adult chronic pain patients are consistently shown to interpret ambiguous health and bodily information in a pain-related and threatening way. This interpretation bias is argued to play a role in the development and maintenance of pain and disability. However, no studies have yet investigated the role of interpretation bias in adolescent pain patients, despite that pain often first becomes chronic in youth. We administered the Adolescent Interpretations of Bodily Threat (AIBT) task to adolescents with chronic pain (N=66) and adolescents without chronic pain (N=74). Adolescents were 10-18 years old and completed the study procedures either at the clinic (patient group) or at school (control group). We found that adolescents with chronic pain were less likely to endorse benign interpretations of ambiguous pain and bodily-threat information than adolescents without chronic pain, particularly when reporting on the strength of belief in those interpretations being true. These differences between patients and controls were not evident for ambiguous social situations, and they could not be explained by differences in anxious or depressive symptoms. Further, this interpretation pattern was associated with increased levels of disability among adolescent patients, even after controlling for severity of chronic pain and pain catastrophizing. The current findings extend our understanding of the role and nature of cognition in adolescent pain, and provide justification for employing the AIBT task in longitudinal and training studies to further investigate causal associations between interpretation bias and chronic pain.

6.1. INTRODUCTION

Cognitive-affective models implicate biased cognitive processes in the etiology and maintenance of chronic pain disorders (Eccleston & Crombez, 1999, 2007; Pincus & Morley, 2001; Todd et al., 2015; Van Damme et al., 2010). Whilst evidence for biased attentional processes is mixed (Crombez et al., 2013; Schoth et al., 2012), studies of interpretation bias have consistently demonstrated robust results (Schoth & Liossi, 2016). Adult chronic pain patients interpret ambiguous information as more indicative of pain and bodily threat compared with controls across a range of tasks (Edwards & Pearce, 1994; Khatibi et al., 2015; McKellar et al., 2003; Pincus et al., 1994, 1996). However, no studies have yet investigated biased interpretations in youth with chronic pain, despite adolescence being regarded as a key developmental period associated with initial pain chronicity (King et al., 2011; Perquin et al., 2000). Studying interpretation bias in adolescent patients could elucidate its role in the early emergence and maintenance of chronic pain, and its potential as a predictor of treatment responsiveness or an intervention target.

To address this empirical gap, we recently developed a new measure to investigate interpretations of ambiguous pain and bodily-threat information in youth: the Adolescent Interpretations of Bodily Threat (AIBT) task (Chapter Five; (Heathcote, Koopmans, et al., 2016)). In this first study, we investigated whether the AIBT task was sensitive to normal variations in pain catastrophizing and acute pain experiences in community adolescents. We showed that the tendency to endorse negative interpretations and to reject benign interpretations of ambiguous vignettes was associated with higher pain catastrophizing and recently experienced pain. This interpretation pattern was not specific for situations regarding pain and bodily threat, but generalized across social situations. This lack of specificity may be because the sample was unselected, and we may expect more specific interpretation biases for bodily threat information in clinical pain samples. It is also unknown whether the

tendency to interpret ambiguous information as being indicative of pain and bodily threat is clinically relevant, that is, associated with poorer functioning in pediatric chronic pain patients, as cognitive-affective models would predict.

In this paper we examine the presence and role of an interpretation bias in adolescents with and without chronic pain. We expected that adolescents with chronic pain would endorse more negative, and less benign interpretations of interpret ambiguous pain and bodily-threat information compared with a control sample of adolescents without chronic pain. We also expected that, unlike in community samples, adolescent patients' bias would not extend to ambiguous social situations. Moreover, given that previous research has shown associations between negative interpretation biases and anxious as well as depressive symptoms in adolescents (Castillo & Leandro, 2010; Creswell, Schniering, & Rapee, 2005; J Hadwin, Frost, French, & Richards, 1997; Orchard, Pass, & Reynolds, 2016a, 2016b; Taghavi, Moradi, Neshat-Doost, Yule, & Dalgleish, 2000), and that young pain patients often report comorbid psychopathology, we explored whether differences between patients and controls would be due to differences in anxious and depressive symptoms. The AIBT task also allows us to assess whether a negative bias is strongest for when patients report whether interpretations come easily to mind (interpretation generation) or how strongly they believe the interpretations to be true (interpretation belief), informing the point in the appraisal process that biases are most influential. If differences between adolescents with and without chronic pain were found in any AIBT task indices, we then examined whether these indices are linearly associated with functional disability among adolescents with chronic pain, beyond what is explained by severity of chronic pain, and by another important cognitive factor, pain catastrophizing.

6.2. METHODS

Participants

Patient group

Adolescents with chronic non-cancer pain were recruited from the Oxford Centre for Children and Young People in Pain (OxCCYP), based at the Nuffield Orthopaedic Centre, part of the Oxford University Hospitals. OxCYPP is part of an orthopaedic musculoskeletal referral system, receiving referrals from gastroenterology, neurology, orthopaedics, spinal units, rheumatology, and General Practitioners. Participants were eligible for the current study if they reported recurrent or persistent pain for more than three months. Participants were also required to be between ages 10 and 18 years, and fluent in English. Patients were excluded if they had current severe mental health issues based on expert clinician judgment by a consultant clinical psychologist. The recruitment period was between October 2014 and April 2016. Participants were recruited as part of a larger study investigating Attention Bias Modification (ABM) training (data reported in Chapter Four), but which involved a baseline phase where we also collected data on interpretation bias. Only data purporting to interpretation bias is reported here. As interpretation biases were measured before training, ABM procedures do not affect data in the current study. Patients and a parent/guardian were first approached about the study either following their first assessment session at the clinic, or following their second visit to the clinic during which they attended a pain education class with a small group of other patients and families. During these sessions, patients and their families were approached by a paediatric rheumatologist or the team's consultant clinical psychologist and asked if they would like to learn more about taking part in a research study. The clinician took verbal consent that the patient and parent/guardian were happy to be approached by a member of the research team, who subsequently provided the information sheet, answered questions about the study, and scheduled appointments. Seventy-three

adolescents and their families were interested in the study, and 67 families agreed to take part. The first participant was recruited as a pilot participant and only completed a small number of measures to examine feasibility of testing in the hospital setting. Thus the final sample comprised 66 adolescent participants (55 female; *M* = 13.97 years; *SD* = 2.13, age range = 10-18 years). Parents/guardians provided informed consent for their children. In addition, participants aged 16 or over provided informed consent for themselves. Participants younger than 16 years provided informed assent. The National Research Ethics Service (NRES), part of the National Health Service (NHS), approved data collection from this patient sample.

Control group

Adolescents in the control group were recruited from two secondary schools in the south of England. The recruitment period was between January and July 2015. Members of the research team contacted schools, and the principals gave verbal consent to make contact with adolescents as potential participants. Teachers of eight school classes then invited all pupils of those classes to take part. Parents of the participants were informed about the study by email, and provided informed consent for their children. In addition, participants aged 16 or over provided informed consent for themselves. Participants younger than 16 years provided informed assent. All participants were fluent in English. These participants were recruited and completed the AIBT task for a previous study to examine associations between interpretation bias and acute pain experiences (i.e., Chapter Five), and the data from this sample is published elsewhere (Heathcote, Koopmans, et al., 2016). For the purposes of the current study, we selected the data from participants in the community sample who did not meet criteria for chronic pain (i.e., those who reported that they had not experienced continuous or recurrent pain for longer than three months). Thus, 74 participants were

selected to be included in the control group for the current study (42 female; *M* = 14.95 years; *SD* = 1.71, age range = 11-18 years). The Central University Research Ethics Committee at the University of Oxford approved data collection from this community sample.

Measures

We collected demographic information to characterise age and gender for both samples. We also collected additional information on demographics and clinical history from the adolescent chronic pain patients to appropriately characterise this sample and allow comparability with other clinical samples in the previous literature. Participants in both samples completed the AIBT task as well as measures of anxiety and depression, and catastrophizing. Only the patients completed the measure of functional disability.

Adolescent Interpretations of Bodily Threat (AIBT) task

The Adolescent Interpretations of Bodily Threat (AIBT) task is a computerized measure of interpretation bias for adolescents (Heathcote, Koopmans, et al., 2016). The task consists of 16 vignettes describing ambiguous situations. Half of the vignettes describe ambiguous situations that may be interpreted as relating to bodily threat or pain, and half describe ambiguous social situations. The situations reflect events that may occur at school, at home, or during everyday adolescent life, including both self-referential and other-oriented items. In the task, participants are first presented with one of the ambiguous situations in the centre of the screen. An example of a bodily threat situation is as follows: *"Your dad jumps out of his chair and puts his hands to his face, making a loud noise. He is…."*. The situation is ambiguous because there are at least two different possible word endings, reflecting different interpretations. The participants are instructed to first read the situation and to

imagine themselves in the situation before pressing the spacebar. After pressing the spacebar, participants are offered one possible end word that resolves the situation in a negative or benign manner. For example, *"Your dad jumps out of his chair and puts his hands to his face, making a loud noise. He is **hurt**"*. An example of a social situation is as follows: "You receive a notification that one of your classmates has put a comment on your picture on Facebook. While opening the webpage you think that it will be something **nice/nasty**." Participants then rate whether that interpretation pops into their mind on a scale of 1 to 5 (1 = doesn't pop into my mind, 3 = might pop into my mind, 5 = definitely pops into my mind). After rating the first word, they are presented with a second word that resolves the situation in a different way; for example, *"Your dad jumps out of his chair and puts his hands to his face, making a loud noise. He is **surprised**"*, and are again asked to rate if that interpretation pops into their mind. Finally, participants are asked to select the interpretation that most easily came to their mind. After the participants have responded to all 16 scenarios, they receive new instructions. Participants are informed that they will see the same situations again, however this time, they are asked to rate their *belief* that each interpretation would actually be happening in that situation (1 = not likely, 3 = maybe likely, 5 = very likely). The addition of this belief question has been used in a number of previous studies to measure interpretation bias in adults and children (e.g., (Clark et al., 1997; Miers et al., 2008)). Bodily threat and social items are presented in a random order that was fixed between participants. Interpretations (i.e., words ending the sentence) are also presented in a fixed random order so that all participants viewed the same order of items and response choices. Participants were not able to go back to previous items after their responses. Participants give a time constraint to complete the AIBT task items.

Functional Disability Inventory

Patients' functional disability was assessed with the Functional Disability Inventory (FDI). This instrument assesses perceived difficulty in performing common activities in the domains of school, home, recreation, and social interactions. Youth rate the difficulty they had in carrying out each activity in the preceding two weeks (0, no trouble; 1, a little trouble; 2, some trouble; 3, a lot of trouble; and 4, impossible). The FDI consists of 15 items and yields a total score that can range from 0 to 60, with higher scores indicating greater disability. The FDI has yielded good reliability and validity for children and adolescents (Walker & Greene, 1991) and for youth with chronic pain (Kashikar-Zuck et al., 2011). Cronbach's alpha in this study was .90 for the total score.

Pain Catastrophizing Scale – Child version

This assessed adolescents' catastrophic thinking about pain (Crombez et al., 2003) and was adapted from the adult Pain Catastrophizing Scale (Michael J. L. Sullivan et al., 1995). It consists of 13 items that yield a total score from 0 to 52. Higher scores indicate more pain catastrophizing. Subscale scores for rumination, magnification, and helplessness can be derived. The PCS-C has good reliability and validity for children above nine years (Crombez et al., 2003). Cronbach's alpha in this study was .88 for the total score.

Pain severity indices

To assess severity of chronic pain, adolescent patients completed one 11-point visual analogue scale indicating their average level of pain in the last 3 months (0 = no pain; 10 = worst pain possible), and one 4-point visual analogue scale indicating their frequency of pain in the last 3 months (1 = on less than one day each month; 6 = every day). These items were

taken from the Brief Pain Inventory (Cleeland & Ryan, 1994), which has been widely used to measure pain experiences in clinical and non-clinical populations.

Revised Child Anxiety and Depression Scale

To assess whether differences in interpretations between adolescents with and without chronic pain were due to differences in generalized anxious or depressive symptomatology, we administered the Revised Child Anxiety and Depression Scale (RCADS (Chorpita et al., 2000)). The RCADS consists of 47 items, scored on a 4-point Likert scale from never to always. Higher scores indicate more anxiety or depression. The RCADS comprises six subscales but in this study we only calculated scores for Generalized Anxiety Disorder and Major Depressive Disorder. The RCADS has yielded good reliability and validity for children and adolescents (Chorpita et al., 2005; Esbjørn et al., 2012; Mathyssek et al., 2013). Cronbach's alpha in this study was .86 for the GAD subscale and .86 for the MDD subscale.

Procedure

The procedure for data collection for the control group and task administration is described in Chapter Five (Heathcote, Koopmans, et al., 2016)) and is therefore not presented again here.

For the school sample (control group), all testing sessions took place at school. For the patient sample, all testing sessions took place at the Nuffield Orthopaedic Centre. After completing the consent/assent forms participants were seated in front of a computer at a distance of approximately 60cm from the screen, to complete the AIBT task. Participants completed two practice trials and the experimenter gave additional verbal instructions for any participants who were unclear (please contact the lead author for a full script). After finishing the AIBT task, participants completed the questionnaire measures. Participants in the patient

group then began the ABM training protocol (to be described elsewhere). Upon completion, participants were debriefed as to the nature of the study. The current study procedure took approximately 45-60 minutes.

Data analysis plan

The AIBT task provides two types of data: 1) ratings of interpretations (i.e., participants' ratings of the different interpretations, in terms of whether they come to mind and their believability, on a scale of 1-5), and 2) forced choice of interpretation (i.e., participants' choice of one interpretation, in terms of whether they come to mind and their believability, for each situation). The ratings data allows us to consider more subtle differences between the endorsement of benign *and* negative interpretations independently, and thus following Chapter Five, we present only the ratings data here. Indeed, inspection of forced choice data reveals broader main effects of group but no interactions with context or block, supporting these assumptions.

Group comparisons

To examine whether interpretations of ambiguous situations differed between adolescents with and without chronic pain (i.e., patient group vs. control group), we performed a multivariate repeated-measures ANOVA. Specifically, we used a 2 x 2 x 2 repeated-measures design with valence (negative/benign word endings), context (bodily threat/social), and block (interpretation generation/belief), as within-subject factors, and group (chronic pain/controls) as a between-subjects factor. A repeated-measures ANOVA was chosen because we were interested in whether the effect of group on both negative and benign interpretations depended on whether participants reported on interpretations coming to

mind (interpretation generation) or their belief in those interpretations being true (interpretation belief) (i.e., block), and whether interpretations varied across context (bodily threat/social situations). Performing a single analysis to investigate these questions afforded the most stringent approach to reduce error from multiple comparisons. If a four-way interaction was found, we first decomposed this interaction to investigate the presence of three-way interactions separately for bodily threat and social items. We chose to decompose four-way interactions this way (i.e., by context) because we hypothesised that chronic pain patients would show biased interpretations specifically for pain and bodily threat information, rather than for social information, whereas all other comparisons (i.e., Valence: negative, benign; Block: generation, belief) were exploratory. Significant findings were subsequently followed by Bonferroni-corrected analyses of simple main effects.

Participants in the patient and control groups differed significantly in age and gender (see *Results*). Thus, if group differences in AIBT task indices were found, we investigated whether age and gender could explain these group differences by exploring whether age and gender were associated with those AIBT task indices. ANOVAs would also be re-run including gender and age as covariates. In addition, if group differences in the AIBT task were found, we investigated whether these differences could be explained by differences in mood by examining whether anxious and depressive symptomatology was associated with the implicated AIBT task indices. ANOVAs would also again be re-run including anxiety and depressive symptomatology as covariates.

Associations with disability

If group differences were identified for any of the AIBT task indices, analyses were then performed to examine whether these indices were linearly associated with disability for adolescents with chronic pain, and whether they could explain unique variance in disability

beyond what is explained by measures of pain severity (pain intensity and frequency in the preceding 3 months) and pain catastrophizing. To do so, we performed multiple hierarchical regression analyses with the relevant AIBT task index entered in the first step, and pain intensity, frequency, and catastrophizing score entered in the second step. Functional disability (FDI) was entered as the dependent variable. FDI data was collected only from adolescents with chronic pain, so we performed this analysis only for the patient sample (N = 66).

Significance testing

For all analyses, $p < .05$ was the cut-off for statistical significance, but exact p values are reported in the text to aid critical interpretation of the data. For the ANOVA analyses, Partial Eta Squared (η_p^2) effect sizes were reported (small effect size = 0.01; medium effect size = 0.06; large effect size = 0.14 (Cohen, 1988; Olejnik & Algina, 2000)). Where assumptions for homogeneity of variance were not met, we reported statistics for equal variances not assumed.

6.3. RESULTS

Participant characteristics

Patient group demographics

Adolescents with chronic pain were predominantly Caucasian (N = 61, 92.4%) and born in the United Kingdom (N = 62, 93.9%). The majority of adolescents had other siblings (N = 59, 89.4%). Most adolescents were attending school full time or had completed schooling (N = 53, 80.3%), although a substantial minority were attending school only part time or receiving home or hospital schooling (N = 12, 18.2%). Time since pain onset varied between 5 and 170 months (M = 45.7 months). Fifty-eight (87.9%) adolescents presented

with widespread musculoskeletal pain, whilst eight (12.1%) presented with pain in only one body location. Most common pain problems included joint pain (*N* = 36, 54.5%), pain in legs or feet (*N* = 35, 53%), back pain (*N* = 33, 50%), and pain in hands or arms (*N* = 30, 45.5%). Twelve participants (18.2%) reported pain all over their body. When asked to indicate the body location where they experienced the most pain, participants most often indicated back pain (*N* = 16, 24.2%), pain in legs or feet (*N* = 15, 22.7%), or joint pain (*N* = 10, 15.2%). Pain onset was reported as gradual for 39 adolescents (59.1%) and sudden for 27 adolescents (40.9%). Adolescents reported a substantial amount of pain (average pain intensity in the last 3 months: *M* = 6.55 out of 10, *SD* = 1.63) and disability (as indexed by Functional Disability Inventory (FDI), *M* = 22.79, *SD* = 10.74). Forty-four adolescents (66.7%) reported experiencing pain every day in the last three months, 20 (30.3%) reported pain on most days, and two (3%) reported pain on about one day per week. Thirty-one (47%) adolescents reported that they had taken pain medication at some point in the weeks leading up to the study.

Demographic group comparisons

Adolescents with and without chronic pain reported similar levels of generalised anxiety (RCADS GAD subscale, Patients: *M* = 6.94, *SD* = 4.25; Controls: *M* = 7.70, *SD* = 3.69; $t(138) = 1.13$, $p = .26$) and depressive symptomatology (RCADS Depression subscale, Patients: *M* = 11.74, *SD* = 5.98, Controls: *M* = 9.99, *SD* = 5.99; ($t(138) = -1.73$, $p = .09$). There were significant differences between adolescents with and without chronic pain in age (Patients: *M* = 13.97, *SD* = 2.13); Controls: *M* = 14.95, *SD* = 1.71; $t(124.38) = 2.96$, p = .004) and gender (Patients: 55 (83.3%) females; Controls: 42 (56.8%) females; $\chi^2 (1) = 11.58$, $p = .001$) (see Group Comparisons section for details on how we controlled for these differences in statistical analyses). Of note, due to a technical fault, data on age was not recorded for one

participant in the control sample. Thus, descriptive statistics of age do not include this participant.

AIBT task results

To examine whether adolescents with and without chronic pain differed in their interpretations of ambiguous situations, a 2 (valence) x 2 (block) x 2 (context) ANOVA was conducted with group (chronic pain vs. controls) as between-subjects factor. The multivariate test yielded main significant effects for **valence**, $F(1, 138) = 10.32$, $p = .002$, $\eta_p^2 = .07$; **context**, $F(1, 138) = 118.11$, $p < .001$, $\eta_p^2 = .46$; and **block**, $F(1, 138) = 42.56$, $p < .001$, $\eta_p^2 = .24$. There was also a significant two-way interaction for **context x group**, $F(1, 138) = 5.43$, $p = .02$, $\eta_p^2 = .04$, for **context x block**, $F(1,138) = 8.93$, $p = .003$, $\eta_p^2 = .06$, and for **block x valence**, $F(1,138) = 80.14$, $p < .001$, $\eta_p^2 = .37$, as well as a significant three-way interaction for **valence x block x context**, $F(1, 138) = 10.60$, $p = .001$, $\eta_p^2 = .07$.

Of greatest relevance for our hypotheses, there were also significant interaction effects with group. Specifically, there was a significant two-way interaction for **valence x group,** $F(1,138) = 4.53$, $p = .04$, $\eta_p^2 = .03$, and a significant four-way interaction for **valence x block x context x group**, $F(1, 138) = 6.39$, $p = .01$, $\eta_p^2 = .04$. All other interactions failed to reach significance (see Table A2 in Appendix G for full description of all main and interaction effects).

To decompose the four-way **valence x block x context x group** interaction, which subsumed all other interactions, we first performed 2 (block) x 2 (valence) ANOVAs with group (chronic pain vs. controls) as between-subjects factor separately for bodily-threat items and social items. These analyses revealed a **valence x block x group** interaction for bodily

threat items $F(1, 138) = 4.91$, p = .03, $\eta_p^2 = .03$, but not for social items $F(1, 138) = 0.89$, $p = .35$, $\eta_p^2 = .01$. Results can be seen in Figure 6.1. Again, all other interactions failed to reach significance (see Table A3 in Appendix G for full description of all main and interaction effects using separate bodily threat and social analyses).

Thus, Bonferroni-corrected analyses of simple main effects were performed for the bodily threat items only, with group (chronic pain vs. controls) as the focus for comparison. These analyses revealed that adolescents with chronic pain were significantly more likely to reject benign interpretations of bodily threat situations when reporting on belief in those interpretations than adolescents without chronic pain ($p = .011$). There were no significant group differences when reporting on whether interpretations came to mind (negative interpretations: $p = .40$; benign interpretations: $p = .16$), or for negative interpretations when reporting on belief in those interpretations ($p = .09$).

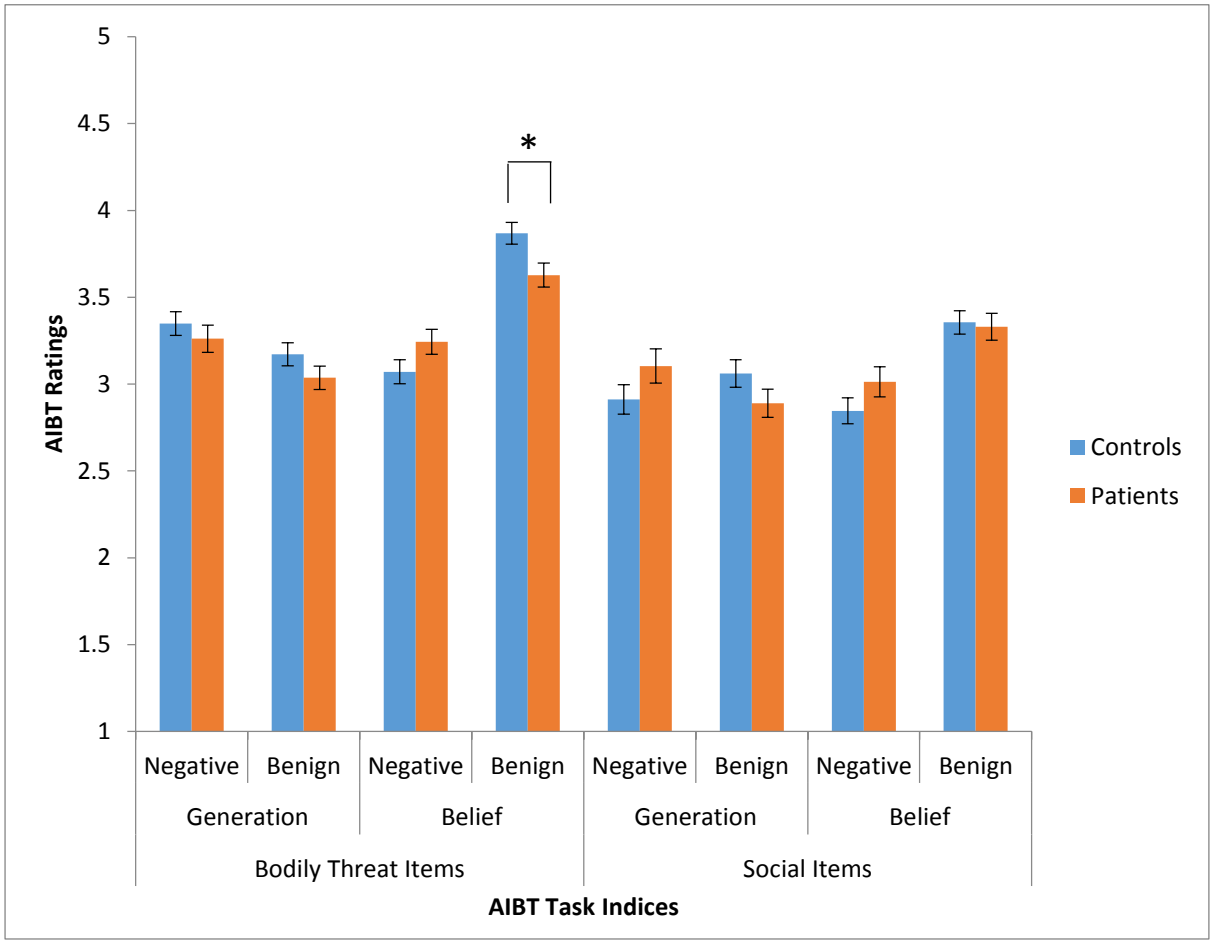


Figure 6.1. AIBT task ratings (error bars = SD, *p <.05)

To examine whether group differences in benign belief items could be explained by group differences in age and gender, we first performed Pearson correlations between age and gender and the benign belief items. These analyses revealed no associations between benign belief items and gender (r = .02, p = .85) or age (r = .16, p = .06), suggesting that group differences in age and gender cannot explain differences in interpretations. We also performed an additional repeated-measures ANOVA as described above, but including age and gender as covariates. In this analysis, the significant four-way **valence x block x context x group** interaction remained significant ($F(1, 135) = 7.09$, p = .009, η_p^2 = .05), again suggesting that group differences in age and gender did not drive effects.

Finally, similar to previous studies (Heathcote, Koopmans, et al., 2016; Pincus et al., 1994), we examined whether group differences in the benign belief items could be explained by anxiety and depressive symptomatology by performing Pearson correlations between anxiety and depression scores and the benign belief items. Again, these analyses revealed no associations between benign belief items and anxiety (r = .02, p = .84) and depressive (r = -.08, p = .36) symptomatology. Of note, though, there were significant associations between the AIBT task social items and anxiety and depressive symptomatology (see Table A4 in Appendix G for correlation table), in line with previous findings from the psychopathology literature (Creswell et al., 2005; Dineen & Hadwin, 2004). In addition, when performing the repeated-measures ANOVA described above again, but including anxiety and depression scores as covariates, the significant four-way **valence x block x context x group** interaction remained significant (F(1,136) = 6.59, p = .011, η_p^2 = .05), again suggesting that AIBT task differences in interpretations between adolescents with and without chronic pain cannot be explained by differences in anxiety and depressive symptomatology.

Associations with disability

Given that group differences on the AIBT task were found, specifically for the belief in benign bodily threat items, we next examined whether this interpretation index was linearly associated with levels of functional disability in the patient sample. We also examined whether this interpretation index explained unique variance in functional disability beyond what is explained by other important factors that have been previously associated with disability; pain intensity, frequency, and catastrophizing. To do so, we conducted a hierarchical multiple regression analysis with belief in benign bodily threat interpretations entered in the first block, and pain intensity, frequency, and catastrophizing scores entered in the second block. Results for the regression analysis are reported in Table 6.1. Specifically,

patient's belief in benign bodily threat interpretations explained a significant amount of the variance in patients' levels of functional disability ($F(1,64) = 5.78$, $p = .019$, $R^2 = .08$). Adding pain intensity, frequency, and catastrophizing (PCS) scores further improved the model ($F(4,61) = 9.12$, $p < .001$; $R^2 = .37$, $p < .001$), however, patients' belief in benign bodily threat interpretations remained a significant predictor of functional disability. Specifically, in the model including all variables, both pain intensity (Beta = .44, $t(61) = 4.12$, $p < .001$) and belief in benign bodily threat interpretations (Beta = -.26, $t(61) = -2.51$, $p = .015$) significantly predicted levels of functional disability, whilst pain catastrophizing score (Beta = .19, $t(61) = 1.77$, $p = .08$), and pain frequency were non-significant (Beta = .06, $t(61) = 0.53$, $p = .60$). This suggests that the index of belief in benign bodily threat interpretations explains unique variance in patients' levels of functional disability even when controlling for severity of chronic pain and pain catastrophizing.

Table 6.1. *Results of hierarchical multiple regression analysis with Functional Disability score (FDI) as the dependent variable*

	b	*SE b*	β
Step 1			
Constant	42.92	8.42	
Belief in benign bodily threat (AIBT index)	-5.52	2.30	-.29*
Step 2			
Constant	9.90	14.83	
Belief in benign bodily threat (AIBT index)	-4.96	1.98	-.26*
Pain frequency (last 3 months)	1.10	2.08	.06
Pain intensity (last 3 months)	2.93	0.71	.44***
Pain Catastrophizing (PCS-C)	0.2	0.11	.19

Note. *$R^2 = .08$ for Step 1 ($p = .02$). $\Delta R^2 = .29$ for Step 2 ($p < .001$).*
**$p < .05$, ***$p < .001$*

6.4. DISCUSSION

In this study we employed the Adolescent Interpretations of Bodily Threat (AIBT) task to compare interpretations of ambiguous information between adolescents with and

without chronic pain. In the task, vignettes describing ambiguous situations that could be interpreted as signifying pain and bodily threat, and those that could be interpreted as negative social situations, are presented. As predicted, adolescents with chronic pain were less likely to endorse benign (i.e., non-threatening) interpretations of ambiguous bodily situations, particularly when reporting on the strength of belief in those interpretations being true. These differences in interpretational style were not evident for social situations, and not statistically explained by differences in anxious or depressive symptoms. Weaker endorsement of benign interpretations was also associated with more functional disability even after statistically controlling for chronic pain severity (indexed by pain intensity and frequency in the preceding 3 months), and pain catastrophizing. These results suggest that interpretations of ambiguity over situations regarding pain and bodily threat were different for adolescents with and without chronic pain, and may be clinically relevant for understanding levels of functioning among adolescent pain patients.

Our findings are consistent with adult studies, which have demonstrated differences between pain patients and controls on a range of interpretation bias tasks. Most of these tasks have used single word stimuli such as homographs and homophones (e.g., pain/pane, terminal) (Pincus et al., 1994, 1996), incomplete word stems (Edwards & Pearce, 1994), or ambiguous facial expressions (Khatibi et al., 2015). The AIBT task used here examines interpretations of more realistic situations that are likely to be encountered in adolescents' lives. Similar vignette-based tasks have been used in previous studies examining associations with pain-related vulnerability constructs in community adult samples (Keogh & Cochrane, 2002; Keogh et al., 2004; Vancleef et al., 2016; Vancleef & Peters, 2008), but not yet with adult chronic pain samples. The AIBT task is also useful for distinguishing whether pain-associated differences arise because of higher ratings of negative interpretations or lower ratings of benign interpretations, as well as differentiating interpretation generation (whether

an interpretation comes to mind) from interpretation belief (belief that the interpretation is true). Our findings suggesting differences only in the endorsement of benign, but not negative interpretations are somewhat out of line with adult studies, which have shown relatively consistently that adults with chronic pain are more likely to interpret ambiguous words and faces in a negative, threat-related way (Schoth & Liossi, 2016). This difference may be due to differences in task parameters. For example, whilst the AIBT task allows for ratings that span a range of certainty, previous studies using single word stimuli have typically measured only which interpretation first comes to mind (e.g., (Pincus et al., 1994, 1996)), which may produce more extreme results. Alternatively, inconsistencies may be due to age differences between the study samples. Nonetheless, our findings are in line with our previous study employing the AIBT task in a community sample of adolescents, where we found that, after controlling for anxious and depressive symptoms, pain-related vulnerability was associated only with rejection of benign, but not endorsement of negative, interpretations. It is important to note, though, that patients in the current study still, on average, reported that benign items were at least somewhat likely to be true (M = 3.63, where '3' = 'maybe likely to be true'). Patients therefore did not outright reject the possibility that benign, instead of bodily-threat interpretations could be true. Differences emerged only in the extent to which patients and controls endorsed benign interpretations, with controls endorsing benign interpretations to a greater extent. Taken together, findings could suggest not only that biased interpretations are a target for treatment, but also, rather than necessarily reducing negative interpretations, interventions that encourage stronger belief in benign interpretations could be potent for adolescent pain patients.

Our findings also extend understanding of cognitive factors in pediatric pain. Previous studies have indicated that youth with chronic pain are characterised by biases in the way they attend to (J. E. Beck et al., 2011; Boyer et al., 2006; Hermann et al., 2008; van der Veek et al., 2014)

and remember (Koutantji et al., 1999) pain-related information. Recent research suggests that biases in attention, memory, and interpretation also characterise community youth who catastrophize about pain (Asmundson et al., 2012; Heathcote et al., 2015; Heathcote, Koopmans, et al., 2016; Noel, Rabbitts, et al., 2015; Vervoort, Trost, & Van Ryckeghem, 2013), suggesting that biases may be relevant for pain-related vulnerability (Noel, Palermo, et al., 2015). We present here evidence that interpretations of ambiguous bodily-threat information are relevant for the experience of chronic pain in youth. It will be important to investigate the role of development in the manifestation and influence of interpretation and appraisal processes across childhood and adolescence. For example, it is interesting that in the current study, group differences emerged only when adolescents reported on their belief in interpretations being true (interpretation belief), rather than whether those interpretations came to mind (interpretation generation). This indicates that adolescents do have the cognitive capacity to differentiate their own interpretations from reality. Future studies could investigate whether changes in cognitive capacity across childhood, adolescence, and adulthood are associated with changes in pain-relevant interpretation processes. It will also be interesting to investigate whether similar findings emerge when adolescents are presented with additional contextual cues that may increase or reduce their belief in their initial interpretations of ambiguous situations.

The current findings are also relevant for the broader literature on cognitive biases and chronic pain. Most work to date has focused on biased attending to pain-related information. In particular, studies highlight the importance of hypervigilance and selective attention for pain (Mohsen Dehghani, Sharpe, & Nicholas, 2003; Heathcote et al., 2015; Vlaeyen & Linton, 2000) interruption by pain (Attridge, Crombez, Van Ryckeghem, Keogh, & Eccleston, 2015; Eccleston & Crombez, 1999), and difficulty disengaging from pain (Eccleston & Crombez, 1999; Khatibi, Dehghani, Sharpe, Asmundson, & Pouretemad, 2009).

Yet, in recent theoretical models, biased attending is proposed as an outcome of biased interpretation, specifically, in the interpretation and appraisal of pain and pain-related information as threatening. For example, the Misdirected Problem-Solving Model (Eccleston & Crombez, 2007) suggests that the belief that pain is harmful and requires a solution will increase the likelihood that patients will classify ambiguous stimuli as pain- and threat-related, and this interpretation bias will in turn enhance attentional capture and interruption by pain, driving avoidance of activities, and thus disability. More recently, Todd and colleagues synthesized prospective and intervention studies to develop the Threat Interpretation Model (Todd et al., 2015). This model proposes that the classification of stimuli as pain- and threat-relevant will lead to a pattern of attentional vigilance-avoidance. Thus, recent reconceptualizations suggest that biases in interpretation may in fact drive biased attending, and may therefore be a more relevant target for intervention (Crombez et al., 2015; Schoth & Liossi, 2016). Relatedly, there already exist novel cognitive training tools that use simple learning mechanisms to encourage more negative or benign interpretations of ambiguous situations (Lau, 2013; MacLeod, 2012; Salemink & Wiers, 2012), and these tools have recently been applied to an experimental pain setting (Jones & Sharpe, 2014).

This study has limitations that we can address in future research. First, this study is cross-sectional, so causal hypotheses are not testable. Frequency effects could explain our findings – that is, chronic pain patients may demonstrate different interpretations of ambiguity simply because of their repeated experiences with bodily pain, poor health, and medical settings. However, if this were the case, we would expect to see group differences in the endorsement of negative interpretations too. Nonetheless, longitudinal studies will be necessary for assessing whether or not interpretations causally predict pain chronicity. It will also be useful to recruit additional control groups, for example adolescents who are tested in a medical setting but who do not have pain. Second, although our findings remained significant

when statistically controlling for anxious and depressive symptoms, it is interesting that our two groups did not differ on these measures (potentially due to the recruitment procedure). Previous studies typically report elevated levels of anxiety and depression in chronic pain samples (Tsang et al., 2008), and our findings remain to be replicated in other clinical and community samples where mood differences may emerge. Also, our two groups did differ on age and sex, and whilst analyses indicated that these factors do not explain current findings, replications with matched samples, in particular from other research groups, are warranted.

In addition to the limitations above, given that the AIBT task items are broadly associated with ill health and bodily threat, we cannot suggest if our findings are reflective of a more specific sensory processing bias in which mild sensations, or ambiguous sensations, are interpreted as painful (Pennebaker, 1982; Pincus et al., 1994). Indeed, this sensory processing bias is most strongly implicated in cognitive-affective models of chronic pain, and may be most relevant for understanding pain chronicity and maintenance. On the other hand, recent models (e.g., (Moseley, 2007)) have emphasised that broader appraisals of bodily threat are also important in chronic pain. Further studies on the specificity of interpretation bias in contributing to chronic pain will be fruitful for comparing and contrasting these models. In addition, whilst our hypothesis that biases would be specific for bodily threat and not social items was driven by cognitive models of pain, previous research has shown that some chronic pain patients report social difficulties and isolation as a consequence of their pain (Snelling, 1994; Strunin & Boden, 2004). The social impact of chronic pain, especially for peer interactions, may be especially relevant in adolescence, in which individuals undergo a process of "social reorientation" entailing increased affiliation with peers, relative to family members (De Lorme et al., 2013; E. E. Nelson et al., 2005). On this basis, we may expect to see interpretation biases that extend to ambiguous social situations in adolescent patients who

have experienced negative social consequences of their pain, and future studies should investigate the role of social factors in bias specificity.

Adolescents with chronic pain, compared with healthy controls, were less likely to endorse benign interpretations of ambiguous bodily-threat information, particularly when reporting on their belief in those interpretations being true. This interpretation pattern was associated with more disability among adolescent patients, even after statistically controlling for severity of chronic pain and pain catastrophizing. The current findings extend our understanding of the role and nature of cognition in adolescent pain, and provide justification for employing the AIBT task in longitudinal and training studies to further investigate causal associations.

Chapter 7

7

Discussion

7.1. Overview

Data presented in this thesis pertain to the roles and plasticity of pain-related cognitive biases, particularly attention and interpretation biases, in adolescents. The studies presented in this thesis address three key questions:

1) Is an attention bias towards pain-related information associated with pain-related vulnerability factors in adolescence, and does attention control moderate this association?

2) Is an attention bias towards pain-related information malleable to change, and can these changes impact pain-related outcomes in adolescents with chronic pain?

3) Is a negative interpretation bias for pain-related and bodily-threat information associated with pain-related vulnerability factors, and chronic pain, in adolescence?

This final chapter briefly summarises each preceding study and synthesises data pertaining to each key question. Findings are then discussed in relation to wider theoretical

and methodological concerns for studying cognitive biases in adolescent pain populations. Finally, recommendations are given for future research to build on the findings presented in this thesis.

7.2. Summary of Results

Chapter Two investigated associations between pain catastrophizing and an attention bias towards pain-related stimuli in a community sample of adolescents, and examined whether attention control moderated associations. Attention bias was measured using a dot-probe task presenting images of adult pain and neutral facial expressions for relatively short (100ms) and longer (1250ms) durations. An attention bias was indexed by relative speeding of response times to identify probes appearing behind pain faces compared with neutral faces. Pain catastrophizing was measured using a self-report questionnaire asking participants to report on how much they normally catastrophize when in pain (the Pain Catastrophizing Scale – Child version (PCS-C); (Crombez et al., 2003)). Attention control was also indexed by a self-report questionnaire, asking participants to report how well they are able to control their attention in everyday life (the Attention Control Scale (ACS); (Derryberry & Reed, 2002)). We found that although there was no direct association between pain catastrophizing and attention bias towards pain faces in adolescents, attention control did significantly moderate this relationship. Although findings did not reach significance when considering lower and higher levels of attention control separately, additional analyses indicated that lower levels of attention control were significantly associated with increasing attentional vigilance towards pain faces only within high catastrophizing adolescents. In addition, we found that poorer attention control was related to increased attention bias for pain faces (regardless of pain catastrophizing level) when these faces were presented for relatively longer durations (i.e., 1250ms) but not for shorter durations (i.e., 100ms).

Chapter Three was designed to build on findings from Chapter Two, with a new community sample of children and adolescents, and employing a stronger methodological design. Attention bias was measured using eye-tracking during a free viewing task in which participants viewed photographs of young people displaying pain (and neutral) facial expressions. Images were presented for 3000ms, and indices of initial fixation and fixation duration were calculated to index relatively early and later stages of attention. Particularly important, participants were informed that the photographs were taken whilst the pictured children completed the cold pressor test (CPT), a task that they would also subsequently complete. Thus, the stimuli were personally relevant for an upcoming pain experience. In addition, state levels of catastrophizing and anxiety in the face of completing the CPT were measured. As in Chapter Two, attention control was measured with the self-report ACS (Derryberry & Reed, 2002). Contrary to the findings presented in Chapter Two, attention control did not moderate associations between pain catastrophizing and attention bias. However, attention control did moderate associations between anxiety and attention bias, particularly regarding how long participants dwelled on pain versus neutral faces. For adolescents reporting low levels of attention control, higher anxiety was associated with less dwell time on pain faces as opposed to neutral faces, and the opposite pattern was observed for adolescents with high attention control. Anxiety and attention control also interacted to predict pain outcomes in the CPT. For adolescents with low attention control, increasing anxiety was associated with anticipating more pain and tolerating pain for less time.

Chapter Four investigated the impact of Attention Bias Modification (ABM) on pain-related attention biases, as well as pain symptomatology, pain catastrophizing, anxiety symptoms, depression symptoms, and disability in adolescents with chronic musculoskeletal pain. As above, pain catastrophizing was measured using the PCS-C (Crombez et al., 2003). Generalised anxiety and depression symptoms were measured using the self-report Revised

Children's Anxiety and Depression Scale (RCADS; (Chorpita et al., 2000)). Disability was measured using the self-report Functional Disability Inventory (FDI; (Walker & Greene, 1991)) as well as two physical tasks (the sit-to-stand task and the cardio wall task). In addition, given the findings presented in earlier chapters, we also investigated the impact of ABM on attention control and whether attention control would moderate training effects. Attention control was indexed using a self-report measure (the ACS (Derryberry & Reed, 2002)) as well as an experimental measure (the Fish Flanker; (Rueda et al., 2004)). Adolescents with chronic pain were randomly assigned to complete eight bi-weekly sessions of dot-probe ABM or placebo training, or to a waitlist control group. Contrary to hypotheses, we found no evidence that ABM training, in comparison to placebo training or waitlist, modified attention bias. Indeed, there was no evidence of an attention bias towards pain-related stimuli in patients at baseline. In addition, we found no impact of ABM training (relative to placebo or waitlist) on pain symptoms or other pain-related outcomes. We also found no evidence that ABM selectively impacted attention control, or that baseline levels of attention control moderated training efficacy.

Chapter Five moved away from the study of attention bias, and instead considered the role of interpretation bias in adolescent pain experiences. We first developed and piloted a novel measure of pain-related interpretation bias in a large community sample of adolescents; the Adolescent Interpretations of Bodily Threat (AIBT) task. The AIBT task presents ambiguous bodily-threat situations, as well as ambiguous social situations. Participants are required to rate benign and negative interpretations for each situation in terms of whether the interpretation comes to mind and whether it is believable. Using this task in a separate community sample of adolescents, we then investigated associations between interpretation bias and pain catastrophizing as well as recent pain experiences. As in previous chapters, pain catastrophizing was measured using the PCS-C (Crombez et al., 2003). Participants also

completed the RCADS (Chorpita et al., 2000) to index anxiety and depression symptoms. Participants also rated their average and worst pain intensity in the past three months (0 = no pain; 10 = worst pain possible), the amount that pain had interfered with their daily activities over the past three months (0 = I don't miss out on any activities; 10 = I miss out on all activities), and the frequency of their pain over the past three months (1 = on less than 1 day each month; 6 = every day) (items taken from the Brief Pain Inventory (BPI); (Cleeland & Ryan, 1994)). We found that adolescents who catastrophize about pain, as well as those who reported more pain issues in the preceding three months, were more likely to endorse negative interpretations, and less likely to endorse benign interpretations, of ambiguous situations. This interpretation pattern was not, however, specific for situations regarding bodily threat, but generalized across social situations as well. We also found that a negative interpretation bias, specifically in ambiguous situations that could indicate bodily threat, mediated the association between pain catastrophizing and recent pain experiences.

Chapter Six was designed to build on findings from Chapter Five by administering the AIBT task to adolescents with chronic pain (n.b., these were the same participants as in the ABM training study), and comparing findings to participants from Chapter Five who reported no pain problems. Adolescents with chronic pain also completed the FDI (Walker & Greene, 1991), BPI (Cleeland & Ryan, 1994), and RCADS (Chorpita et al., 2000) to index functional disability, severity of chronic pain, and anxiety and depression symptoms, respectively. We found that adolescents with chronic pain were less likely to endorse benign interpretations of ambiguous bodily-threat information than adolescents without chronic pain, particularly when reporting on the strength of belief in those interpretations being true. These differences between patients and controls were not evident for ambiguous social situations, and they could not be explained by differences in anxious or depressive symptoms. Further, this interpretation pattern was significantly associated with increased levels of disability among

adolescent patients, even after controlling for severity of chronic pain and levels of pain catastrophizing.

7.3. Considerations and Future Directions for Studies on Attention Bias

7.3.1. Summary of Findings

Data reported in Chapters Two, Three, and Four address the first two key questions outlined in this thesis:

1) Is an attention bias towards pain-related information associated with pain-related vulnerability factors in adolescence, and does attention control moderate this association?

2) Is an attention bias towards pain-related information malleable to change, and can these changes impact pain-related outcomes in adolescents with chronic pain?

Taken together, we found no evidence that an attention bias towards pain-related information is directly associated with pain catastrophizing, anxiety in the face of pain, or tolerance and experience of experimentally-induced pain in community samples. Data indicates that this is the case even when using diverse methodologies to index attention bias such as response times on the dot-probe task, and eye-tracking indices on a free viewing task. Data also indicates that this is the case when considering both trait pain catastrophizing (i.e., catastrophizing when generally experiencing pain) as well as state catastrophizing and anxiety in the face of an upcoming pain experience. We also found no evidence that adolescent chronic pain patients selectively attended to pain versus neutral information. These findings are out-of-line with cognitive-affective models of chronic pain which propose that chronic pain patients will be characterised by an attention bias towards pain-related information, and that there will be direct associations between attention bias and other

vulnerability factors such as pain-related anxiety and catastrophizing (e.g., (Eccleston & Crombez, 1999, 2007; Pincus & Morley, 2001)). However, findings from Chapters Two and Three do indicate that attention control moderates the association between attention bias and pain catastrophizing, as well as pain-related anxiety. Moreover, findings from Chapter Three indicate that attention control is also an important moderator of the association between anxiety and pain tolerance, indicating that associations between anxiety and attention control may be relevant for understanding behavioural outcomes. Thus, we provide evidence from two separate studies that attention control is an important moderator of the association between attention bias and cognitive-affective, as well as behavioural, responses to pain. However, findings are not entirely consistent between the studies presented in Chapters Two and Three; there are three discrepant findings that particularly warrant further consideration.

First, whilst we found no evidence that participants had an overall attention bias towards pain-related stimuli in Chapter Two, we did find that participants displayed an overall attention bias towards pain-related stimuli in Chapter Three. This inconsistency may be explained by differences in the salience of pain-related stimuli between studies. That is, whilst photographs of pain facial expressions were not personally relevant for participants' own pain experiences in Chapter Two, they were directly relevant for an upcoming pain experience in Chapter Three. Thus, it is likely that the photographs were more salient for participants in Chapter Three, and thus more likely to capture attention. This is also in line with a motivational account of attention to pain (e.g., (Van Damme et al., 2010)), indicating that pain-related information will only capture attention if it is personally relevant to the individual's immediate goals, in this case, gathering information about an upcoming pain experience (the CPT).

Second, whilst attention control moderated the association between attention bias and *catastrophizing* in Chapter Two, it instead moderated the association between attention bias

and *anxiety* in Chapter Three. Attention control did not significantly moderate the association between attention bias and catastrophizing in Chapter Three. Both pain catastrophizing and pain-related anxiety have been implicated as vulnerability factors in cognitive-affective models of chronic pain, and both are proposed to associate with pain-related attending (Asmundson et al., 2012; Vlaeyen & Linton, 2000). The inconsistency between findings in Chapters Two and Three may therefore again be explained by methodological differences between studies. For example, whilst Chapter Two investigated more trait-like pain catastrophizing (i.e., levels of catastrophizing when experiencing pain in everyday life), Chapter Three investigated state catastrophizing in the face of an upcoming pain task (the CPT). It may be that the CPT does not engender catastrophic thoughts and beliefs to the same extent that naturally-induced pain can do outside of the laboratory. For example, participants may expect that an experimenter would not ask them to complete a pain task that could have long-term damaging effects on body tissue. In addition, participants in Chapter Three were informed that they could remove their hand from the water whenever they could no longer tolerate the pain. The ability to immediately remove a source of pain may be less possible in the case of naturally-occurring pain, where tissue damage can take longer to heal. Indeed, participants in Chapter Three reported relatively low levels of state catastrophizing (M = 15.81, range = 0-60). Instead, state anxiety symptoms may better reflect participants' emotional response to experimentally-induced pain. Indeed, whilst the CPT may not engender catastrophic beliefs, it may still stimulate anxious symptomatology such as feeling nervous, jittery, and frightened. Indeed, although participants still reported relatively low levels of anxiety (M = 12.20), mean levels were relatively elevated when considering the lower possible range of scores for state anxiety (range = 0-40) than for state catastrophizing (range = 0-60).

Third, the direction of effects was different across Chapters Two and Three. Particularly, in Chapter Two, higher levels of catastrophizing were associated with *increased* selective attending towards pain faces in participants with low levels of attention control. However, in Chapter Three, higher levels of anxiety were associated with *decreased* selective attending towards pain faces in participants with low levels of attention control. Once again, findings could be due to methodological differences between the two studies. For example, as suggested above, pain face stimuli were likely more salient for participants in Chapter Three. Relatedly, it is also important to note that, in comparison to Chapter Two, there was no evidence of *avoidance* of pain faces in Chapter Three. Indeed, in Chapter Three, differences in low versus high attention control were reflected only in a smaller attention bias towards pain faces, but not attentional avoidance of pain faces. This inconsistency may be explained by the fact that dot-probe and eye-tracking methodologies index different components of attentional processing. Indeed, we found that findings were not different across stimulus presentation times in Chapter Two, and we therefore calculated a combined index of relatively earlier and later processing. In contrast, in Chapter Three, findings were different across relatively early (initial fixation) and later (fixation duration) attentional eye-tracking indices, with effects of anxiety and attention control found only for later stages of attention (i.e., overall dwell time). However, it is also important to note that initial fixations on pain stimuli (as indexed by eye-tracking) may not be similar to attending towards stimuli presented for 100ms (as indexed by the dot-probe). Indeed, whilst the 100ms stimulus presentation time was selected to reflect relatively early stages of attentional processing in Chapter Two, studies in the broader attention bias literature often employ even shorter presentation times (e.g., 10-20ms) and normally using masked stimuli (e.g., (Bradley, Mogg, & Lee, 1997)) to tap into initial, involuntary attentional capture. Thus, a presentation time of 100ms may not be sufficient to index very early, initial attention fixations. Although these

alternative interpretations cannot be teased apart using the current dataset, future studies employing eye-tracking methodology whilst participants complete a dot-probe task may be useful to disentangle dynamic attentional processes and to provide evidence for where the task indices overlap.

Fourth, whilst attention control was identified as a significant moderator of findings in Chapters Two and Three, it did not moderate ABM training efficacy in Chapter Four. This is perhaps surprising given that findings from Chapters Two and Three indicate that attention control plays an important role in associations between attention bias and pain-related outcomes. Indeed, from a dual process perspective (Derryberry & Reed, 2002), it is the combination of biased attending towards pain, and low attention control, that is most likely to lead to negative pain-related outcomes. We may therefore expect that ABM training would be particularly useful for adolescents with low baseline levels of attention control. However, findings from Chapter Four did not support this hypothesis. In addition, given that ABM has been suggested to directly target effortful attention control processes (Browning, Holmes, Murphy, et al., 2010), it is perhaps surprising that ABM training also did not impact levels of attention control. This apparent inconsistency may be due to the absence of pain-related attention biases in adolescent patients at baseline. In addition, it may be because ABM did not effectively manipulate attention bias in our patients, thus precluding any possibility of moderation effects based on individual cognitive factors. Alternatively, our selected measures of attention control may not have been sensitive to detect changes across training time. For example, whilst the ACS (Derryberry & Reed, 2002) may provide a useful measure of trait-like attention control, it may not be sensitive to incremental changes following attention-related training, and thus may not provide a useful outcome measure. In addition, whilst the Flanker task has been demonstrated to be a sensitive outcome measure in previous attention-related training studies (Rueda, Rothbart, McCandliss, Saccomanno, & Posner, 2005; Wang,

Richard, & Schmular, 2014), it may not be relevant for understanding associations between pain-related attention and pain outcomes. As we included only the ACS (Derryberry & Reed, 2002) in Chapters Two and Three, it is unknown whether flanker data would also moderate associations between pain-related attention bias and other pain-related vulnerability factors. Indeed, whilst the ACS (Derryberry & Reed, 2002) is argued to provide a general measure of attentional focus and switching in a variety of everyday situations, the Flanker task is argued to index attentional interference by unrelated task distractors. It may be that the ability to focus and switch one's attention in complex daily situations is most relevant for understanding pain-related outcomes. Moreover, tasks that index attention control in the face of pain stimuli may be more sensitive to changes following ABM, and could be included in future studies. Nonetheless, if ABM is shown to impact attention in patients who display an attention bias at baseline, or if training tools are developed that better manipulate attention biases, it will be interesting to investigate the potential moderating role of attention control in these studies.

7.3.2. Future Directions

There are a number of research questions that remain to be addressed, and could usefully be considered in future research on pain-related attention bias in adolescents.

First, it is unclear whether data presented in Chapters Two and Three truly reflect pain-specific processes, or whether they reflect a vulnerability factor that is shared in other areas of emotional and physical health. For example, an attention bias for pain-related information (in this case, facial expressions) may simply reflect a general tendency to attend towards (or avoid) threat. Future studies may consider using non-pain threat stimuli (e.g., angry faces), in addition to pain stimuli, to better examine whether or not pain-related vulnerability is associated specifically with biased attentional processing of pain-related

information, or more broadly of threat-related information. As discussed in Chapter One, a small number of studies have measured attentional biases towards social threat stimuli in young people with chronic pain (J. E. Beck et al., 2011; Boyer et al., 2006). Although findings are somewhat inconsistent across the studies, there is some evidence that youth with chronic pain are characterised by attention biases for social as well as pain-related threat (J. E. Beck et al., 2011; Boyer et al., 2006). Relatedly, given that a threat-related attention bias is implicated in the aetiology of paediatric anxiety disorders (Bar-Haim, Lamy, Pergamin, Bakermans-Kranenburg, & van IJzendoorn, 2007), that anxiety is associated with pain catastrophizing in community and clinical paediatric samples (Crombez et al., 2003), and that anxiety-linked processes are broadly considered as vulnerability factors in adult and paediatric psychological models of chronic pain (Asmundson et al., 2012; Vlaeyen & Linton, 2000), it may be that findings across Chapters Two and Three are driven by underlying anxiety mechanisms. As we did not administer measures of trait anxiety in Chapters Two and Three, we cannot test this hypothesis using the current dataset. Whilst we did measure state anxiety in Chapter Three, the measure was administered in the face of an upcoming pain task, and thus may not reflect generalised anxious pathology. Future studies may include measures of trait anxiety to better examine specificity of associations between attention bias and cognitive-affective outcomes within the context of pain. In addition, there is also evidence that biased attentional processes are associated with other emotional disorders such as depression (Browning, Holmes, Charles, Cowen, & Harmer, 2012; Platt, Waters, Schulte-Koerne, Engelmann, & Salemink, 2016) as well as broader personality factors such as defensiveness (Franklin, Holmes, Smith, & Fowler, 2016), neuroticism (Goubert, Crombez, & Van Damme, 2004), and behavioural inhibition (Muris et al., 2007). Thus, it will also be important for future studies to consider not only the role of co-occurring anxiety, but also

other personality and psychological vulnerability factors associated with poorer outcomes, especially across development.

Second, there are methodological considerations regarding the selection of stimuli for attention bias tasks. The adaptation of facial stimuli in Chapter Three, specifically to increase relevance of stimuli for a personal pain experience, provided a significant advance in methodological design. However, facial stimuli still may not elicit processes of pain-related attending that are most relevant for understanding chronic pain outcomes. Whilst it is assumed that biased attending towards cues for *personal* pain experiences are most relevant for understanding chronic pain aetiology, facial stimuli arguably tap into other-oriented pain responses. Attending towards another person in pain may better reflect empathic tendencies than a tendency to attend towards one's own pain sensations, or cues for personal pain experiences. On the other hand, it has recently been argued that viewing another person in pain activates concerns for personal pain-related threat, and thus initiates similar escape and avoidance tendencies as for pain cues that are directly related to one's own bodily integrity (Vervoort & Trost, 2015). Within this interpersonal framework, facial pain stimuli may be considered adequate proxy stimuli of a personal pain-related threat.

Third, there are methodological considerations regarding the selection of attention bias tasks. In Chapter Two we employed dot-probe methodology; however our findings indicated poor split-half reliability. Poor reliability of the dot-probe task is also reported elsewhere in the pain (Dear et al., 2011b) and psychopathology (Schmukle, 2005) literatures. In addition to issues regarding reliability, dot-probe methodology can only index attentional processes indirectly, using response times. Eye-tracking methodology employed in Chapter Three was thus chosen to provide a more direct measure of visual attention, and to allow investigation of more dynamic attentional processes (e.g., initial fixations versus dwell time). However, the free-viewing task used to generate eye-tracking indices is also limited in that it

captures only visuospatial attentional processing of static stimuli. Other tasks may be more useful for illuminating different components of pain-related attending, as well as for mapping attentional processes more directly onto the cognitive mechanisms proposed to underlie pain-related vulnerability. For example, difficulties in shifting attention *away* from negative information is considered a core cognitive process underlying worry and rumination (Koster, De Lissnyder, & De Raedt, 2013). As worry and rumination about pain are proposed as core components of pain catastrophizing (Michael J. L. Sullivan et al., 1995), it may be that pain catastrophizing is most strongly associated with biased attending towards pain-related information held in working memory. Within the psychopathology literature, new tasks have been developed to specifically index attentional processes associated with worry and rumination. For example, Koster and colleagues (Koster et al., 2013) recently developed the Internal Switching Task (IST), in which participants are presented with a series of (visual) threat-related and neutral stimuli, and are required to hold a count of each stimulus type in their working memory. The task is self-paced so that participants make a motor response (i.e., press a button) once they have updated their mental count. In a university student sample, Koster and colleagues (Koster et al., 2013) found that increased levels of rumination were related to attentional switching impairments (as indexed by slower response times on switch trials), specifically in the context of threatening information. Of particular importance, the IST demonstrated high internal consistency and test-retest reliability (Koster et al., 2013). Thus, future studies may consider adapting this task to investigate attentional switching between pain-related and non-pain information in adolescents with varying levels of pain catastrophizing.

Fourth, there are methodological considerations regarding the measurement of pain outcomes. In Chapter Three we used the CPT to index experiential and behavioural responses to thermal (cold pressor) pain. The CPT has been well validated in children and young people

(Birnie, Petter, Boerner, Noel, & Chambers, 2012). However, given that thermal pain is less common than other types of pain in everyday life (e.g., musculoskeletal pain, incisive pain), it is unknown how well our results reflect pain experiences outside of the laboratory. Future studies may consider employing alternative experimental pain induction techniques that mirror more everyday pain (e.g., a Delayed Onset Muscle Soreness (DOMS) paradigm to induce muscle pain (e.g., (Niederstrasser et al., 2014))). However, there will be a trade-off between ecological validity and precision of experimental manipulation (e.g., controlling for individual differences in muscle strength, and enabling rapid pain cessation to index tolerance). Alternatively, future studies may consider employing non-experimental paradigms such as diary measures (Van Ryckeghem et al., 2013) and Ecological Momentary Assessment (EMA) (Moskowitz & Young, 2006) that may better indicate attentional capture by pain in everyday life. These measures may be especially relevant for chronic pain populations (e.g., (Garcia-Palacios et al., 2014)).

Finally, given that we found no evidence that ABM effectively changed pain-related attending in adolescents with chronic pain, future studies may consider using different experimental designs to investigate causal associations between attention bias and pain outcomes. Importantly, as we found no evidence of an overall attention bias towards pain in our patient sample, a first step may be to selectively recruit patients who display a bias towards pain. Novel, more reliable tasks (e.g., an adapted version of the IST (Koster et al., 2013)) will be particularly important. If these novel tasks provide strong evidence that pain-related attention biases characterise youth with chronic pain, we can then better investigate causal processes. Adapting (reliable) measurement tasks into training tasks, as with dot-probe-based ABM, is one option. However, it will also be useful to investigate whether treatments that are currently used in routine clinical care (e.g., Cognitive Behavioural Therapy (CBT) (Fisher et al., 2014)) also impact attentional processes, albeit indirectly. In

addition, mindfulness-based interventions, which are receiving growing attention for the treatment of chronic pain, place purposeful control of attention as a central treatment mechanism (Chiesa & Serretti, 2011). We may therefore expect that pain-related attention bias would change following a mindfulness intervention. Interestingly, Petter and colleagues (Petter, McGrath, Chambers, & Dick, 2014) have provided preliminary evidence that a mindfulness-based attention manipulation improves experimental pain outcomes in adolescents who regularly practice meditation, however they did not investigate whether attention biases were also impacted by the intervention.

In summary, there are a number of theoretical and methodological issues that remain to be addressed in future studies. The development of tasks that reliably index pain-related attending is paramount, as well as tasks that are designed to index more specific cognitive processes (e.g., worry and rumination about pain). The study presented in Chapter Four of this thesis, as well as previous adult studies in clinical pain populations (Sharpe et al., 2012), have failed to show that ABM can effectively change patterns of pain-related attending. Thus, it will be important to consider the utility of different experimental paradigms for investigating the plasticity and causal impact of pain-related attention biases, including the measurement of attention bias following evidence-based interventions that are known to at least partially target attention.

7.4. Considerations and Future Directions for Studies on Interpretation Bias

7.4.1. Summary of Findings

Data reported in Chapters Five and Six address the third key question outlined in this thesis:

3) Is a negative interpretation bias for pain-related and bodily-threat information associated with pain-related vulnerability factors, and chronic pain, in adolescence?

Taken together, the studies presented in Chapters Five and Six provided evidence that interpretations of ambiguous information are associated with pain-related vulnerability factors in adolescent community samples, and with the experience of chronic pain in youth. Interestingly, repeated-measures analyses revealed that whilst higher levels of pain catastrophizing were associated with a tendency to endorse negative and to reject benign interpretations of broadly ambiguous information in community samples, the experience of chronic pain in youth was associated with a more specific bias for bodily-threat information. In particular, adolescents with chronic pain significantly differed from adolescents without chronic pain only in their level of belief for benign interpretations of bodily-threat information. These findings are in line with the content-specificity hypothesis that guides much research on cognitive biases in psychopathology (A. T. Beck, 1976).

Unlike the studies presented in Chapters Two and Three, we also investigated whether associations between interpretation bias and pain-related factors were significant even after controlling for symptoms of generalised anxiety and depression. It is interesting that, in Chapter Two, findings remained significant only for benign, but not negative interpretations after controlling for symptoms of anxiety and depression. This is particularly interesting given that group differences between patients and controls, as indicated in Chapter Six, were also found only for benign, but not negative, interpretations (also after statistically controlling for levels of anxiety and depression). Whilst these findings require replication, they indicate that future studies may benefit from further examining how adolescents with pain, and those who are vulnerable for developing pain, attribute benign interpretations to ambiguous bodily-

threat information, perhaps in longitudinal designs. In addition, it may be particularly useful for future studies to investigate interpretation processes in adolescents who do and do not have comorbid anxiety disorders and/or depression. In adult samples, there is some evidence that patients with chronic pain and comorbid depression demonstrate stronger negative interpretation biases for health-related information than patients with chronic pain but without depression (Rusu, Pincus, & Morley, 2012). Given that anxiety disorders are more commonly comorbid with chronic pain in youth (Campo et al., 2004; Chorney et al., 2011; Lipsitz et al., 2005), it will be interesting to see if these findings also replicate in samples of adolescent chronic pain patients with and without a comorbid anxiety disorder.

7.4.2. Future Directions

There are a number of research questions that remain to be addressed, and could usefully be considered in future research on interpretation bias in adolescent pain populations.

First, whilst pain-related vulnerability factors are more consistently associated with interpretation than attention biases in this thesis, this is perhaps unsurprising given that both interpretation bias and other pain-related vulnerability factors (e.g., pain catastrophizing) are typically measured using self-report, and may overlap in terms of cognitive processes. Indeed, common method variance, and potential item overlap, may partially explain extant associations between interpretation bias and pain catastrophizing. However, given that we also found associations between interpretation bias and recent pain experiences, as well as associations between interpretation bias and disability in adolescent patients, overlapping measurement of cognitive processes is unlikely to entirely explain findings. In addition, as we found differences in interpretation patterns between adolescent patients and controls, common method variance is also unlikely to entirely explain findings. Nonetheless, it will be

important to investigate associations between interpretation biases and behavioural pain outcomes (e.g., tolerance of experimentally-induced pain) in future adolescent samples. Additionally, a number of experimental interpretation bias tasks have recently been developed that do not depend on self-report (e.g., (Khatibi et al., 2015; Vancleef et al., 2016)). These tasks could be usefully employed in adolescent populations going forward.

Second, one important consideration for the study of pain-related interpretation bias is the paradox of pain-related ambiguity. In studies within the context of psychopathology, stimulus ambiguity is considered vital to elicit interpretation biases. Indeed, an ambiguous stimulus must have multiple possible interpretations, both negative and benign, to be relevant for studying individual differences in patterns of interpretation. Given that pain is an evolutionarily-primed signal of threat, one could argue that no pain experience is truly ambiguous. Thus, the study of pain-related interpretation bias is a complex one. In this thesis, we developed a task that parallels tasks typically used in the study of paediatric anxiety (e.g., (Miers et al., 2008)), thus permitting comparability across pain and psychopathology literatures. Specifically, we developed and piloted a large number of short vignettes describing ambiguous situations, and selected those which elicited both negative and benign interpretations from adolescent school students. However, as the experience of pain is rarely considered ambiguous, the vignettes that were selected for the final AIBT task are better considered as relating to health and bodily threat, rather than pain sensations per se. Whilst our findings indeed indicate that interpretations of bodily threat are relevant for understanding pain in youth, it will be important to develop alternative tasks to better understand and tease apart the role of appraisal and interpretation in adolescent sensory pain experiences. One option is to draw from the conditioning literature, particularly studies investigating generalisation of conditioned responses to novel, ambiguous stimuli (e.g., (Till & Priluck, 2000)). For example, one could pair two different sensory stimuli (e.g.,

vibrotactile stimuli) with either a painful sensation or no pain. An 'ambiguous' stimulus could then be created by morphing the two non-painful conditioned stimuli, and interpretation bias could be indexed by self-report (e.g., 'how likely do you think this stimulus will lead to pain') as well as behavioural outcomes (e.g., avoidance).

Third, as in the study of pain-related attention bias, future research should employ designs that better investigate the causal contribution of interpretation bias to pain experiences. Longitudinal designs will be useful for examining whether or not biased interpretations precede the onset of chronic pain disorders. In particular, it may be useful to administer the AIBT task in a sample of adolescents awaiting surgery, as there is evidence that these young people are at risk for the development of chronic pain (Rabbitts, Groenewald, Tai, & Palermo, 2014). Indeed, in line with a diathesis-stress framework (Turk, 2002), we may expect that a negative pain-related interpretation bias will only contribute to the development of chronic pain following an acute injury or an initial episode of acute pain. Intervention studies will also be useful. In line with the earlier discussion on attention biases, it will be useful to examine whether interpretation biases are malleable to change, and thus whether they could be a therapeutic target. As with ABM paradigms, tasks that are used to measure interpretation biases (e.g., ambiguous situation tasks) could be adapted into training tasks. Indeed, Jones and colleagues (Jones & Sharpe, 2014) revealed that an ambiguous scenarios training task, in which adult participants were trained to have either a threatening or non-threatening interpretation of pain-related scenarios, successfully manipulated patterns of pain-related interpretation bias. Importantly, adult participants trained to have a threatening interpretation of pain also hesitated more before performing a CPT (i.e., took longer to immerse their hand in the cold water), providing initial evidence that interpretation biases may be causally associated with pain experiences, at least in adults. Alternatively, given that CBT is already used in the treatment of paediatric chronic pain (Fisher et al., 2014), and that

CBT is designed in part to target maladaptive appraisal processes (Thorn, 2004), it will be useful to investigate if interpretation biases also change following CBT for adolescents with chronic pain.

In summary, there are a number of theoretical and methodological issues that remain to be addressed in future studies. As for the study of attention bias, it will be important to consider the utility of different experimental paradigms for investigating the plasticity and causal impact of pain-related interpretation biases. This includes the investigation of changes in interpretation bias following evidence-based interventions that are known to target appraisals (e.g., CBT). In addition, studies employing tasks that do not rely on self-report will be useful to overcome shared method variance and item overlap for studying associations with psychological correlates of pain, such as pain catastrophizing. Finally, theoretical considerations of the paradox of pain-related ambiguity, and implications for task selection in this field, will be valuable.

7.5. General Future Directions

In addition to the points above, there are also a number of considerations for future research that cut across the studies presented in this thesis, and pertain to the broader study of cognitive biases in adolescent pain experiences.

7.5.1. What about Memory?

Studies presented in this thesis have considered the occurrence, nature, and psychological correlates of pain-related attention and interpretation biases in adolescents. Whilst biases in attention and interpretation are most implicated in cognitive-affective models of chronic pain (e.g., (Aldrich et al., 2000; Eccleston & Crombez, 1999; Todd et al., 2015; Van Damme et al., 2010; Vlaeyen & Linton, 2000), this thesis would be remiss without

consideration of a third process; memory bias. As with the study of attention and interpretation biases in pain populations, the study of pain-related memory bias has been greatly informed by the psychopathology literatures. Within a psychopathological framework, it is generally argued that individuals will show a propensity to remember material that is congruent with their current mood state, or with their primary disorder (Bradley, Mogg, & Millar, 1996; K Mogg, Mathews, & Weinman, 1987). Similarly, it is argued that individuals with chronic pain will selectively remember pain-related information over non-pain information (Pincus & Morley, 2001). Memories for pain are, in turn, argued to have important long-term consequences for subsequent health behaviours and pain perception, for example by increasing anxiety and fear responses in the face of pain, and promoting avoidance of future painful events (Noel, Chambers, Petter, et al., 2012). Interestingly, pain-related memory biases were the focus of very early studies on cognitive biases in adult pain populations (see (Pincus & Morley, 2001)), although researchers have generally focused on attention and interpretation biases in more recent years.

Memory bias paradigms employed in adult pain populations have tended to measure the free recall of pain-related versus neutral words. Studies have typically revealed enhanced recall of pain-related relative to neutral words in adult patients with chronic pain, compared to healthy controls, particularly when the words are encoded in self-referential ways (see (Pincus & Morley, 2001) for a review of early studies). Interestingly, as in the study of interpretation bias, there is also preliminary evidence that pain-related memory bias is enhanced in patients with comorbid chronic pain and depression (Pincus, Pearce, McClelland, & Isenberg, 1995), although findings remain to be replicated. One published study to date employed a recall task to study pain-related memory bias in youth with chronic pain. Specifically, Koutantji and colleagues (Koutantji et al., 1999) found that paediatric chronic pain patients recalled significantly more pain words than controls when those words had been

encoded as relevant to the self, however similar effects were also found for neutral words. Thus, at present, there is little evidence for selective recall of pain words in youth pain populations. However, paediatric pain researchers have also begun to consider memory for actual pain experiences in childhood, and findings from these studies are more revealing. For example, some authors (e.g., (Noel, Chambers, Petter, et al., 2012)) have conceived of pain-related memory bias as a deviation in recall from initial pain reports (i.e., following an experimental or clinical pain procedure), leading to either an over- or under-estimation of pain. A pain-related memory bias is thus typically computed as a difference score between initial and recalled pain (Noel, Chambers, McGrath, Klein, & Stewart, 2012). Using this approach, children and adolescents who exhibit a negative pain-related memory bias have been shown to be at risk for experiencing increases in distress and pain over time (Chen, Zeltzer, Craske, & Katz, 2014; Noel, Rabbitts, et al., 2015). In addition, Noel and colleagues (Noel, Ms, et al., 2012) have revealed that children with higher state anxiety during an experimental pain procedure (the CPT) had more negative pain memories, again suggesting a contributory role of anxiety in pain-related cognitive biases in youth. Interestingly, Noel and colleagues (Noel, Ms, et al., 2012) also found that state anxiety uniquely predicted children's pain memories over and above other well-established factors such as anxiety sensitivity and fear of pain, partially reflecting our findings presented in Chapter Three.

In addition to considering a role of memory bias in adolescent pain, it is also important to note that cognitive biases are not proposed to exist in isolation. Indeed, psychological models of chronic pain (Pincus & Morley, 2001) typically propose that biases in attention, interpretation, and memory will causally impact one another, and will interact in their contribution to the development and maintenance of chronic pain. Whilst the relationship and interaction of cognitive biases was not a focus of this thesis, it will undoubtedly form an important avenue for future research. Although it is not yet well studied

in the context of pain, a combined cognitive bias hypothesis is receiving increased attention in the psychopathology literatures. For example, Hirsch and colleagues (Hirsch, Clark, & Mathews, 2006) proposed a first model of the interplay of cognitive processes in social phobia, and Everaert and colleagues (Everaert, Koster, & Derakshan, 2012) have proposed a similar model for depression. Intriguingly, cognitive control processes, including attention control, are considered alongside cognitive biases in these models. Under this framework, studies presented in this thesis provide some of the first evidence for a combined cognitive bias hypothesis in the field of pain. However, studies investigating the interplay between attention, interpretation, and memory biases will also be important. In particular, paradigms that can track patterns of attending, interpreting, and remembering within the same task (e.g., (Everaert, Duyck, & Koster, 2014)) will be particularly useful for capturing their additive and interactive effects on pain experiences.

7.5.2. Developmental Issues

Developmental considerations have guided much of the research presented in this thesis. Primarily, the steep increase in the onset of chronic pain during adolescence (Perquin et al., 2000) suggests that studies investigating this developmental stage may be particularly important for understanding the early development and maintenance of chronic pain. This consideration guided the recruitment of adolescent samples for all studies in this thesis. In addition, examination of attention control processes in Chapters Two through Four was guided, in part, by evidence indicating protracted development of these processes during adolescence. That is, although investigation of attention control processes is warranted within the broader context of dual process models (e.g., (Derryberry & Reed, 2002)), they may be particularly interesting to study within developmental populations. In particular, given the developmental importance of mastery over attention in adolescence [10; 36], and that there is

protracted neuro-development of brain regions engaged in goal-directed attention during adolescence [36; 38; 47], individual differences in the rate of development may contribute to greater vulnerability. However, the role of child development was not a central focus in this thesis. The studies presented mostly cross-sectional data, and all longitudinal data (i.e., Chapter Three) were collected within a brief time frame to investigate causal rather than developmental processes. We included age as a covariate in additional analyses, which revealed no interactions with main findings. However, given that studies were not designed to disentangle developmental processes, this is perhaps unsurprising. Nonetheless, a number of research avenues will be important for increasing our understanding of the role of child development in cognitive-affective contributions to pain.

First, we require larger cross-sectional studies recruiting samples that span childhood, adolescence, and adulthood. These studies could help identify when pain-related cognitive biases first emerge, and when they first associate with pain-related vulnerability factors. These studies may also unravel the unique contributions of age, pubertal status, and disease stage (e.g., duration of pain) in chronic pain disorders. Second, as discussed in all chapters above, longitudinal studies will be particularly powerful for disentangling temporal associations between pain, affect, and cognition. Third, future studies should investigate mechanisms underlying the early emergence of pain-related cognitive biases. Studies have already identified how pain-related beliefs and behaviors may be learnt by observing others (Goubert, Vlaeyen, Crombez, & Craig, 2011). Relatedly, the family environment has been identified as an important context for understanding, assessing, and managing paediatric pain (Palermo et al., 2014). It is perhaps unsurprising, therefore, that parental behaviour has been shown to influence experimental pain outcomes in children (Christine Therese Chambers, 2003), and it will likely influence the emergence and maintenance of pain-related cognitive biases in youths. Noel and colleagues (Noel, Rabbitts, et al., 2015) have provided some

preliminary work showing that parental catastrophizing about child pain is the strongest predictor of children's affective pain memories, over and above the child's own emotional response to pain. However, experimental studies are needed to directly examine the transmission of pain-related cognitive biases from parents to children. As before, relevant experimental paradigms have been developed within the context of psychopathology (e.g., (Remmerswaal, Muris, & Huijding, 2015)), and these paradigms could be usefully adapted for the study of paediatric pain. In addition, studies examining familial aggregation of pain-related cognitive biases, particularly in clinical samples, will be revealing.

7.5.3. Understanding Pain-Related Cognitive Biases in Other Populations[1]

This thesis has focused on the study of pain in community samples, and in adolescent patients with chronic non-cancer pain. The research designs employed in this thesis have also been largely guided by theoretical models of chronic non-cancer pain (e.g., (Eccleston & Crombez, 1999; Pincus & Morley, 2001; Vlaeyen & Linton, 2000)). However, it is surprising that cognitive-affective processes have been largely ignored within the study of cancer-related pain to date, both in adults and in youth. In this final section I will argue that the study of pain-related cognitive biases within the context of cancer, particularly for individuals in survivorship, provides an ideal model for furthering our understanding of cognitive biases and threat-perception to the human experience of pain.

Forty years ago, three quarters of adults and children diagnosed with cancer died. Today, almost half of adults (Quaresma, Coleman, & Rachet, 2015) and three quarters of children survive (Cancer Research UK, n.d.; National Cancer Intelligence Network, 2012). Survival,

[1]An extended version of this section has been submitted and is currently under review as follows: **Heathcote, L. C.,** & Eccleston, C. (under review). Pain and cancer survival: A cognitive-affective model of symptom appraisal and the uncertain threat of disease recurrence.

however, is rarely psychologically simple. Life after cancer is typically characterised by an altered relationship with embodied perception: in particular an anxious uncertainty about the meaning of new or recurrent sensations such as pain (Cioffi, 1991; Pennebaker, 1982, 2000). Cancer survival is an altered context in which pain can make one fear the worst (Crist & Grunfeld, 2013). Indeed, in this stage, the important – often long hoped for – communication that potentially life-shortening disease is no longer active is often accompanied by an instruction or desire to monitor and be vigilant for potential symptoms of recurrence (Macmillan Cancer Support, n.d.). This instruction primes for attention to altered and new physical sensations, and can be accompanied by the suggestion to take a '*better safe than sorry'* strategy in appraising sensations as threatening (Bellizzi, Latini, Cowan, DuChane, & Carroll, 2008; Lee-Jones, Humphris, Dixon, & Hatcher, 1997). The challenge of this caring message is that pain is not only a common feature of cancer survival (Glare et al., 2014; Hudson et al., 2003), and can be chronic (Burton, Fanciullo, Beasley, & Fisch, 2007; Glare et al., 2014; Levy, Chwistek, & Mehta, 2008; Peuckmann et al., 2009), but is also a normal part of leading an active, healthy life. This message may be particularly impactful in the transition from adolescence to adulthood, during which the responsibility to evaluate signs and symptoms of recurrence, such as pain, may move from the caregiver to the young survivor. In addition, as the period of adolescence and its transition into young adulthood is crucial for pubertal and sexual maturation, brain and cognitive development, and the acquisition of a stable self-identity (Spear, 2000a), any effects of cancer during adolescence could hold devastating effects on these growth trajectories. Yet, as this developmental juncture has also been regarded as a period of increased opportunity to flourish (Blakemore & Choudhury, 2006), it could also reflect a key turning point away from negative outcomes through the acquisition of more adaptive, healthy habits and behaviours.

To date, research on the experience of pain in cancer survival has existed largely within a biological frame. That is, pain is studied as the result of tissue damage from the cancer itself or from surgery, chemotherapy, or radiotherapy (Brown, Ramirez, & Farquhar-Smith, 2014; Glare et al., 2014). There are almost no studies on the unique experience of acute, everyday pain in cancer survival. We know very little about whether and how habits of attending, interpreting, and reporting on physical symptoms such as pain are established, maintained, or extinguished, or how these habits influence subsequent pain experience. We also know very little about whether cognitive biases following cancer are associated with the gross behaviours we measure in clinical studies, such as clinic attendance, medication use, and coping behaviours such as emotion-regulation, avoidance, and help-seeking. Cognitive bias after cancer, in the context of '*better safe than sorry'*, is similar but different to chronic non-cancer pain, and should be understood as a particular problem of managing extreme *uncertainty* in the face of an improbable but potentially life-threatening danger. In survival, one is motivated to believe that the pain is non-threatening, but can find it hard to continually judge a true from a false alarm. It is a context defined by the uncertainty of threat, and a lack of easy access to objective threat assessment. Such environments are high risk for the development of anxiety and maladaptive coping (Costanzo, Ryff, & Singer, 2009; Deimling, Bowman, Sterns, Wagner, & Kahana, 2006; Mehnert & Koch, 2008). Below, I propose the Cancer Threat Interpretation Model (see Figure 1 below), a cognitive-affective model of the appraisal and experience of pain in the context of cancer survival.

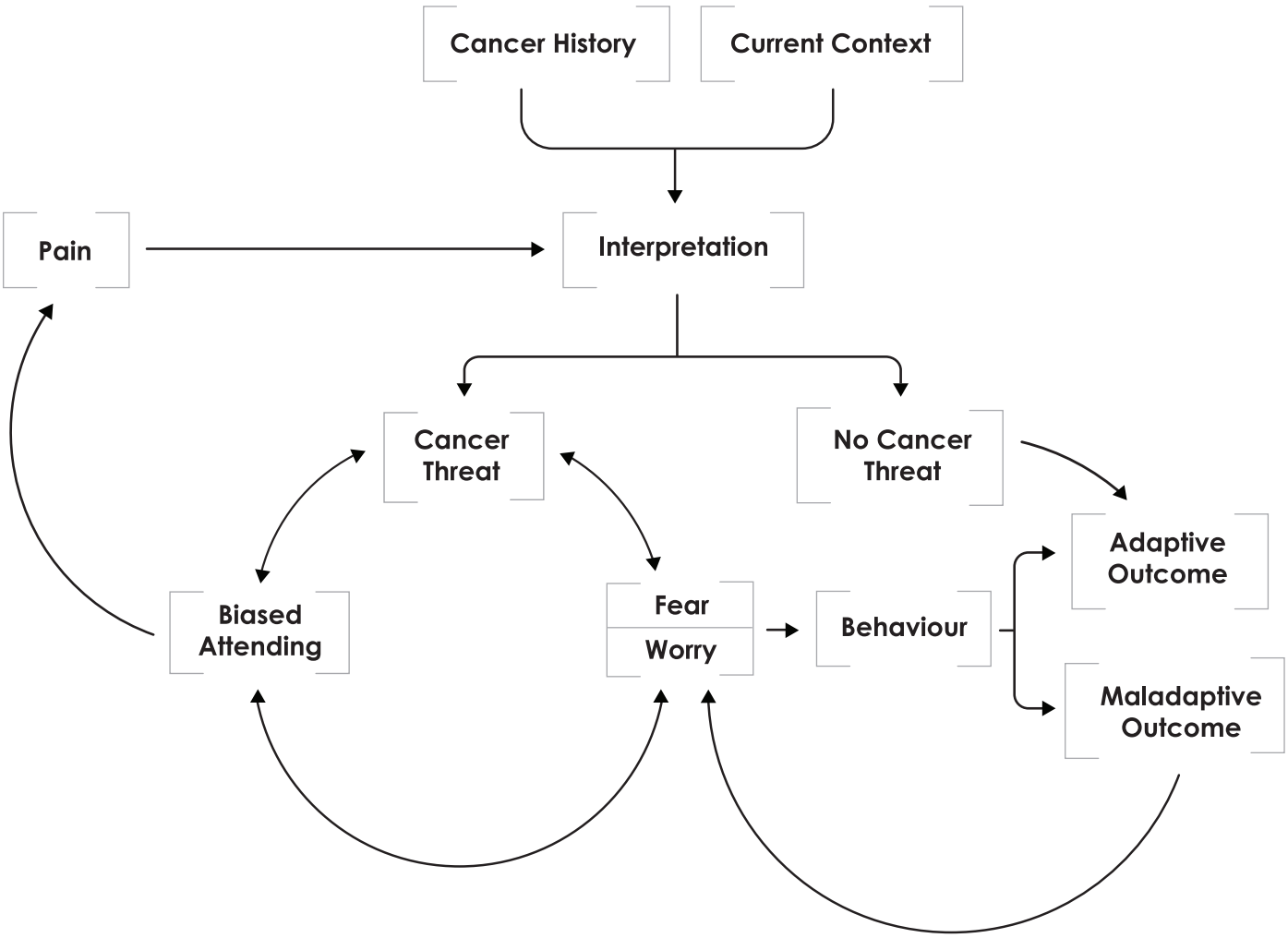


Figure 1. The Cancer Threat Interpretation Model. The model begins with pain, which demands interpretation (cancer threat or no cancer threat). This interpretation depends on the individual's cancer history (e.g., was pain a key feature of diagnosis?), the current context (e.g., is there a clear cause of the pain?), and the interaction between the two (e.g., is the current pain similar to the previous cancer pain?). It is also in the current context, and its interaction with cancer history, where uncertainty emerges. If no cancer threat is determined, there can be an adaptive outcome. Of note, our model refers only to cancer-specific outcomes, and we recognise that non-cancer related maladaptive outcomes can result from pain outside of this context. If a cancer threat is determined, there will be biased attending (hypervigilance, monitoring, difficulty disengaging), fear, and worry, which will maintain one another, and in turn amplify the experience of pain. To alleviate fear and worry, behaviours will be selected. We include here behaviours typically measured in clinical studies (e.g., help-seeking, clinic attendance, avoidance), as well as cognitive coping strategies (e.g., emotion regulation). The choice of behaviour, whether adaptive or maladaptive, will lead to recovery or will enhance fear and worry, maintaining the cycle of biased cognition and fear.

The Cancer Threat Interpretation Model has a number of research implications; of which we highlight just four. (1) If cognitive biases do underpin both threat appraisal and coping following pain, then it begins with interpretation. It is not clear the extent to which the style of interpreting pain as threatening becomes habitual, although it is likely driven by the individual's experience of pain at diagnosis and during treatment, the clinical instruction received at remission, and trait-like individual differences. (2) Relatedly, although we know a lot about the mechanisms of attending to experimentally-induced and chronic non-cancer pain (Aldrich et al., 2000; Crombez et al., 2013; Eccleston & Crombez, 1999, 2007; Heathcote et al., 2015; Van Damme et al., 2010), it is not clear how far cancer-related pain achieves and maintains attentional capture. Cognitive tasks used in this thesis could be usefully employed in cancer survivor populations. (3) Also important to understanding threat appraisal and attending is a better understanding of the context of threat. There are excellent studies on living with uncertainty following cancer (e.g., (Hall, Mishel, & Germino, 2014; Parry, 2003; Sammarco, 2001; Wonghongkul, Dechaprom, Phumivichuvate, & Losawatkul, 2006)), but less studied is how this uncertainty influences pain, alters cognitive-affective responses, and subsequent behavioural outcomes. (4) The behavioural consequences of this cognitive-affective view offer evidence of the motivated output of threat appraisal, including the role of clinic attendance, demand for diagnostic tests, and avoidance, as well as cognitive coping strategies such as emotion regulation and re-appraisal. Whilst previous research has focused on measuring the incidence of chronic pain in survivor populations (Burton et al., 2007), also important are acute episodes of pain and intense worry. We predict that acute episodic experiences will be most guided by threat-related biases, and will have an equal impact on help seeking.

In summary, the consideration of pain-related cognitive biases in cancer survivor populations, particularly in the transition from adolescence to adulthood, provides a unique

and promising opportunity for furthering our understanding in this field. In particular, it provides a valuable opportunity to understand pain-related cognitive biases within the context of threat-perception and motivation, and places the understanding of these processes within a 'normal' psychology of pain.

7.6. Conclusions

Pain is common during adolescence and can impair functioning. Given the deleterious impact and burden of pediatric chronic pain, research is needed to better understand causal and contributory factors during this developmental period. The studies presented in this thesis have contributed to existing knowledge relating to developmental risk factors for chronic pain disorders in adolescence, as well as psychological factors that may contribute to acute and everyday pain experiences in healthy adolescents. Findings provide preliminary evidence for a role of attention and interpretation biases in adolescent pain experiences, including in chronic pain disorders. Findings stand to inform future interventions for adolescents who struggle with pain problems, and in doing so, to improve outcomes for these young people.

8

References

Aldrich, S., Eccleston, C., & Crombez, G. (2000). Worrying about chronic pain: vigilance to threat and misdirected problem solving. *Behaviour Research and Therapy*, *38*(5), 457–470. http://doi.org/10.1016/S0005-7967(99)00062-5

Alfano, C. a, Zakem, A. H., Costa, N. M., Taylor, L. K., & Weems, C. F. (2009). Sleep problems and their relation to cognitive factors, anxiety, and depressive symptoms in children and adolescents. *Depression and Anxiety*, *26*(6), 503–12. http://doi.org/10.1002/da.20443

Ameringer, S. (2010). Barriers to pain management among adolescents with cancer. *Pain Management Nursing*, *11*(4), 224–233. http://doi.org/10.1016/j.pmn.2009.05.006

Armstrong, T., & Olatunji, B. O. (2012). Eye tracking of attention in the affective disorders: A meta-analytic review and synthesis. *Clinical Psychology Review*. http://doi.org/10.1016/j.cpr.2012.09.004

Asmundson, G. J. G., Carleton, R. N., & Ekong, J. (2005). Dot-probe evaluation of selective attentional processing of pain cues in patients with chronic headaches. *Pain*, *114*(1-2), 250–256. http://doi.org/10.1016/j.pain.2004.12.025

Asmundson, G. J. G., & Hadjistavropoulos, H. D. (2007). Is High Fear of Pain Associated With Attentional Biases for Pain-Related or General Threat? A Categorical Reanalysis. *Journal of Pain*, *8*(1), 11–18. http://doi.org/10.1016/j.jpain.2006.05.008

Asmundson, G. J. G., Noel, M., Petter, M., & Parkerson, H. A. (2012). Pediatric fear-avoidance model of chronic pain: Foundation, application and future directions. *Pain Research and Management*, *17*(6), 397–405.

Attridge, N., Crombez, G., Van Ryckeghem, D., Keogh, E., & Eccleston, C. (2015). The Experience of Cognitive Intrusion of Pain. *Pain*, *156*(10), 1978–1990. http://doi.org/10.1097/j.pain.0000000000000257

Bagwell, C. L., Newcomb, A. F., & Bukowski, W. M. (1998). Preadolescent friendship and peer rejection as predictors of adult adjustment. *Child Development*, *69*(1), 140–153. http://doi.org/10.1111/j.1467-8624.1998.tb06139.x

Bakker, F. C., Van Wieringen, P. C. W., Van der Ploeg, H. M., & Spielberger, C. D. (1989). *Handleiding bij de Zelfbeoordelingsvragenlijst voor Kinderen (ZBVK).* Lisse, The Netherlands: Swets & Zeitlinger.

Bardeen, J. R., & Orcutt, H. K. (2011). Attentional control as a moderator of the relationship between posttraumatic stress symptoms and attentional threat bias. *Journal of Anxiety Disorders*, *25*(8), 1008–1018. http://doi.org/10.1016/j.janxdis.2011.06.009

Bar-Haim, Y. (2010). Research Review: Attention bias modification (ABM): A novel treatment for anxiety disorders. *Journal of Child Psychology and Psychiatry and Allied Disciplines*, *51*(8), 859–870. http://doi.org/10.1111/j.1469-7610.2010.02251.x

Bar-Haim, Y., Lamy, D., Pergamin, L., Bakermans-Kranenburg, M. J., & van IJzendoorn, M. H. (2007). Threat-related attentional bias in anxious and nonanxious individuals: a meta-analytic study. *Psychological Bulletin*, *133*(1), 1–24. http://doi.org/10.1037/0033-2909.133.1.1

Baron, R. M., & Kenny, D. a. (1986). The moderator-mediator variable distinction in social psychological research: conceptual, strategic, and statistical considerations. *Journal of Personality and Social Psychology*, *51*(6), 1173–1182. http://doi.org/10.1037/0022-3514.51.6.1173

Baum, C., Schneider, R., Keogh, E., & Lautenbacher, S. (2013). Different stages in attentional processing of facial expressions of pain: A dot-probe task modification. *Journal of Pain*, *14*(3), 223–232. http://doi.org/10.1016/j.jpain.2012.11.001

Beard, C. (2011). Cognitive bias modification for anxiety: current evidence and future directions. *Expert Review Neurotherapy*, *11*(2), 299–311. http://doi.org/10.1586/ern.10.194.Cognitive

Beck, A. T. (1976). *Cognitive Therapy and the Emotional Disorders*. *Cognitive therapy and the emotional disorders* (Vol. 8). http://doi.org/10.1016/S0005-7894(77)80293-1

Beck, J. E., Lipani, T. a., Baber, K. F., Dufton, L., Garber, J., Smith, C. a., & Walker, L. S. (2011). Attentional bias to pain and social threat in pediatric patients with functional abdominal pain and pain-free youth before and after performance evaluation. *Pain*, *152*(5), 1061–1067. http://doi.org/10.1016/j.pain.2011.01.029

Beesdo, K., Knappe, S., & Pine, D. S. (2009). Anxiety and anxiety disorders in children and adolescents: developmental issues and implications for DSM-V. *The Psychiatric Clinics of North America*, *32*(3), 483–524. http://doi.org/10.1016/j.psc.2009.06.002

Belli, S. R., & Lau, J. Y. F. (2014). Cognitive Bias Modification Training in Adolescents: Persistence of Training Effects. *Cognitive Therapy and Research*, *38*(6), 640–651. http://doi.org/10.1007/s10608-014-9627-7

Bellizzi, K. M., Latini, D. M., Cowan, J. E., DuChane, J., & Carroll, P. R. (2008). Fear of Recurrence, Symptom Burden, and Health-Related Quality of Life in Men With Prostate Cancer. *Urology*, *72*(6), 1269–1273. http://doi.org/10.1016/j.urology.2007.12.084

Bernstein, A. (2013). System and method for monitoring and training attention allocation. Google Patents. Retrieved from http://www.google.com/patents/WO2013157012A1?cl=en

Birnie, K. a, Caes, L., Wilson, A. C., Williams, S. E., & Chambers, C. T. (2014). A practical guide and perspectives on the use of experimental pain modalities with children and adolescents. *Pain Management*, *4*(2), 97–111. http://doi.org/10.2217/pmt.13.72

Birnie, K. a, Petter, M., Boerner, K. E., Noel, M., & Chambers, C. T. (2012). Contemporary use of the cold pressor task in pediatric pain research: a systematic review of methods. *The Journal of Pain : Official Journal of the American Pain Society*, *13*(9), 817–26. http://doi.org/10.1016/j.jpain.2012.06.005

Blakemore, S. J., & Choudhury, S. (2006). Development of the adolescent brain: Implications for executive function and social cognition. *Journal of Child Psychology and Psychiatry and Allied Disciplines*. http://doi.org/10.1111/j.1469-7610.2006.01611.x

Boston, A., & Sharpe, L. (2005). The role of threat-expectancy in acute pain: Effects on attentional bias, coping strategy effectiveness and response to pain. *Pain*, *119*(1-3), 168–175. http://doi.org/10.1016/j.pain.2005.09.032

Boyer, M. C., Compas, B. E., Stanger, C., Colletti, R. B., Konik, B. S., Morrow, S. B., & Thomsen, A. H. (2006). Attentional biases to pain and social threat in children with recurrent abdominal pain. *Journal of Pediatric Psychology*, *31*(2), 209–220. http://doi.org/10.1093/jpepsy/jsj015

Bradley, B. P., Mogg, K., & Lee, S. C. (1997). Attentional biases for negative information in

induced and naturally occurring dysphoria. *Behaviour Research and Therapy*, *35*(10), 911–927. http://doi.org/10.1016/S0005-7967(97)00053-3

Bradley, B. P., Mogg, K., & Millar, N. (1996). Memory bias in clinical and nonclinical depression. *Behaviour Research and Therapy*, *34*(11-12), 865–879. http://doi.org/10.1016/S0005-7967(96)00074-5

Brown, M. R., Ramirez, J. D., & Farquhar-Smith, P. (2014). Pain in cancer survivors. *British Journal of Pain*, *8*(4), 139–53. http://doi.org/10.1177/2049463714542605

Browning, M., Holmes, E. a, & Harmer, C. J. (2010). The modification of attentional bias to emotional information: A review of the techniques, mechanisms, and relevance to emotional disorders. *Cognitive, Affective & Behavioral Neuroscience*, *10*(1), 8–20. http://doi.org/10.3758/CABN.10.1.8

Browning, M., Holmes, E. a., Charles, M., Cowen, P. J., & Harmer, C. J. (2012). Using attentional bias modification as a cognitive vaccine against depression. *Biological Psychiatry*, *72*(7), 572–579. http://doi.org/10.1016/j.biopsych.2012.04.014

Browning, M., Holmes, E. A., Murphy, S. E., Goodwin, G. M., & Harmer, C. J. (2010). Lateral Prefrontal Cortex Mediates the Cognitive Modification of Attentional Bias. *Biological Psychiatry*, *67*(10), 919–925. http://doi.org/10.1016/j.biopsych.2009.10.031

Brun Sundblad, G. M., Saartok, T., & Engstrom, L. M. T. (2007). Prevalence and co-occurrence of self-rated pain and perceived health in school-children: Age and gender differences. *European Journal of Pain*, *11*(2), 171–180. http://doi.org/10.1016/j.ejpain.2006.02.006

Burton, A. W., Fanciullo, G. J., Beasley, R. D., & Fisch, M. J. (2007). Chronic pain in the cancer survivor: a new frontier. *Pain Medicine (Malden, Mass.)*, *8*(2), 189–198. http://doi.org/10.1111/j.1526-4637.2006.00220.x

Caes, L., Vervoort, T., Eccleston, C., Vandenhende, M., & Goubert, L. (2011). Parental catastrophizing about child's pain and its relationship with activity restriction: The mediating role of parental distress. *Pain*, *152*(1), 212–222. http://doi.org/10.1016/j.pain.2010.10.037

Campo, J. V, Bridge, J., Ehmann, M., Altman, S., Lucas, A., Birmaher, B., … Brent, D. A. (2004). Recurrent abdominal pain, anxiety, and depression in primary care. *Pediatrics*, *113*(4), 817–824. http://doi.org/10.1542/peds.113.4.817

Cancer Research UK. (n.d.). Children's cancers survival statistics. Retrieved April 1, 2016, from http://www.cancerresearchuk.org/health-professional/cancer-statistics/childrens-cancers/survival#heading-Zero

Carlbring, P., Apelstrand, M., Sehlin, H., Amir, N., Rousseau, A., Hofmann, S. G., & Andersson, G. (2012). Internet-delivered attention bias modification training in individuals with social anxiety disorder - a double blind randomized controlled trial. *BMC Psychiatry*, *12*(1), 66. http://doi.org/10.1186/1471-244X-12-66

Carleton, R. N., Asmundson, G. J. G., Collimore, K. C., & Ellwanger, J. (2006). Strategic and automatic threat processing in chronic musculoskeletal pain: a startle probe investigation. *Cognitive Behaviour Therapy*, *35*(4), 236–247. http://doi.org/10.1080/16506070600898504

Carleton, R. N., Richter, A. a., & Asmundson, G. J. G. (2011). Attention Modification in Persons with Fibromyalgia: A Double Blind, Randomized Clinical Trial. *Cognitive Behaviour Therapy*, *40*(4), 279–290. http://doi.org/10.1080/16506073.2011.616218

Castillo, M. D., & Leandro, P. G. (2010). Interpretation bias in anxiety a synthesis of studies with children and adolescents. *Procedia - Social and Behavioral Sciences*, *5*, 1105–1111. http://doi.org/10.1016/j.sbspro.2010.07.243

Chambers, C. T. (2003). The impact of maternal behaviour on children's pain experiences: An experimental analysis. *Dissertation Abstracts International: Section B: The Sciences*

and Engineering, *63*(3), 293–301. http://doi.org/10.1093/jpepsy/27.3.293
Chambers, C. T., McGrath, P. J., Gilbert, C. A., & Craig, K. D. (1996). *Child facial coding system - revised manual*. Halifax, NS, Canada: IWK-Grace Health Centre, Dalhousie University & University of British Columbia.
Chen, E., Zeltzer, L. K., Craske, M. G., & Katz, E. R. (2014). Children's memories for painful cancer treatment procedures: implications for distress. *Child Development*, *71*(4), 933–947. http://doi.org/10.2307/1132335
Chiesa, A., & Serretti, A. (2011). Mindfulness-based interventions for chronic pain: a systematic review of the evidence. *Journal of Alternative and Complementary Medicine (New York, N.Y.)*, *17*(1), 83–93. http://doi.org/10.1089/acm.2009.0546
Chorney, J. M., Crofton, K., & McClain, B. C. (2011). Theories on Common Adolescent Pain Syndromes. In B. C. McClain & S. Suresh (Eds.), *Handbook of Pediatric Chronic Pain* (pp. 27–44). Springer.
Chorpita, B. F., Moffitt, C. E., & Gray, J. (2005). Psychometric properties of the Revised Child Anxiety and Depression Scale in a clinical sample. *Behaviour Research and Therapy*, *43*(3), 309–322. http://doi.org/10.1016/j.brat.2004.02.004
Chorpita, B. F., Yim, L., Moffitt, C., Umemoto, L. a., & Francis, S. E. (2000). Assessment of symptoms of DSM-IV anxiety and depression in children: A revised child anxiety and depression scale. *Behaviour Research and Therapy*, *38*(8), 835–855. http://doi.org/10.1016/S0005-7967(99)00130-8
Christ, S. E., Kester, L. E., Bodner, K. E., & Miles, J. H. (2011). Evidence for selective inhibitory impairment in individuals with autism spectrum disorder. *Neuropsychology*, *25*(6), 690–701. http://doi.org/10.1037/a0024256
Christensen, M. F., & Mortensen, O. (1975). Long-term prognosis in children with recurrent abdominal pain. *Archives of Disease in Childhood*, *50*(2), 110–114. http://doi.org/10.1136/adc.50.2.110
Cioffi, D. (1991). Beyond attentional strategies: cognitive-perceptual model of somatic interpretation. *Psychological Bulletin*, *109*(1), 25–41. http://doi.org/10.1037/0033-2909.109.1.25
Clark, D. M., Salkovskis, P. M., Ost, L. G., Breitholtz, E., Koehler, K. a, Westling, B. E., … Gelder, M. (1997). Misinterpretation of body sensations in panic disorder. *Journal of Consulting and Clinical Psychology*, *65*(2), 203–213. http://doi.org/10.1037/0022-006X.65.2.203
Clarke, P. J. F., Notebaert, L., & MacLeod, C. (2014). Absence of evidence or evidence of absence: reflecting on therapeutic implementations of attentional bias modification. *BMC Psychiatry*, *14*, 8. http://doi.org/10.1186/1471-244X-14-8
Cleeland, C. S., & Ryan, K. M. (1994). Pain assessment: global use of the Brief Pain Inventory. *Annals of the Academy of Medicine Singapore*.
Cohen, J. (1988). *Statistical power analysis for the behavioral sciences*. *Statistical Power Analysis for the Behavioral Sciences* (Vol. 2nd). http://doi.org/10.1234/12345678
Cohen Kadosh, K., Heathcote, L. C., & Lau, J. Y. F. (2014). Age-related changes in attentional control across adolescence: how does this impact emotion regulation capacities? *Frontiers in Psychology*, *5*, 111. http://doi.org/10.3389/fpsyg.2014.00111
Costanzo, E. S., Ryff, C. D., & Singer, B. H. (2009). Psychosocial adjustment among cancer survivors: findings from a national survey of health and well-being. *Health Psychology : Official Journal of the Division of Health Psychology, American Psychological Association*, *28*(2), 147–156. http://doi.org/10.1037/a0013221
Craig, K. D. (2009). The Social Communication Model of Pain. *Canadian Psychology*, *50*(1), 22–32. http://doi.org/10.1037/a0014772
Creswell, C., Schniering, C. A., & Rapee, R. M. (2005). Threat interpretation in anxious

children and their mothers: Comparison with nonclinical children and the effects of treatment. *Behaviour Research and Therapy*, *43*(10), 1375–1381. http://doi.org/10.1016/j.brat.2004.10.009

Crist, J. V., & Grunfeld, E. A. (2013). Factors reported to influence fear of recurrence in cancer patients: A systematic review. *Psycho-Oncology*. http://doi.org/10.1002/pon.3114

Crombez, G., Bijttebier, P., Eccleston, C., Mascagni, T., Mertens, G., Goubert, L., & Verstraeten, K. (2003). The child version of the pain catastrophizing scale (PCS-C): A preliminary validation. *Pain*, *104*(3), 639–646. http://doi.org/10.1016/S0304-3959(03)00121-0

Crombez, G., Eccleston, C., Baeyens, F., & Eelen, P. (1998). When somatic information threatens, catastrophic thinking enhances attentional interference. *Pain*, *75*(2-3), 187–198. http://doi.org/10.1016/S0304-3959(97)00219-4

Crombez, G., Eccleston, C., Van Damme, S., Vlaeyen, J. W. S., & Karoly, P. (2012). Fear-avoidance model of chronic pain: the next generation. *The Clinical Journal of Pain*, *28*(6), 475–83. http://doi.org/10.1097/AJP.0b013e3182385392

Crombez, G., Heathcote, L. C., & Fox, E. (2015). The puzzle of attentional bias to pain : beyond attention. *Pain*, *156*(9), 1581–1582.

Crombez, G., Van Ryckeghem, D. M. L., Eccleston, C., & Van Damme, S. (2013). Attentional bias to pain-related information: A meta-analysis. *Pain*, *154*(4), 497–510. http://doi.org/10.1016/j.pain.2012.11.013

De Lorme, K., Bell, M. R., & Sisk, C. L. (2013). The Teenage Brain: Social Reorientation and the Adolescent Brain--The Role of Gonadal Hormones in the Male Syrian Hamster. *Current Directions in Psychological Science*, *22*(2), 128–133. http://doi.org/10.1177/0963721413479607

Dear, B. F., Sharpe, L., Nicholas, M. K., & Refshauge, K. (2011a). Pain-related attentional biases: The importance of the personal relevance and ecological validity of stimuli. *Journal of Pain*, *12*(6), 625–632. http://doi.org/10.1016/j.jpain.2010.11.010

Dear, B. F., Sharpe, L., Nicholas, M. K., & Refshauge, K. (2011b). The psychometric properties of the dot-probe paradigm when used in pain-related attentional bias research. *J Pain*, *12*(12), 1247–1254. http://doi.org/10.1016/j.jpain.2011.07.003

Dehghani, M., Sharpe, L., & Nicholas, M. K. (2003). Selective attention to pain-related information in chronic musculoskeletal pain patients. *Pain*, *105*(1-2), 37–46. http://doi.org/10.1016/s0304-3959(03)00224-0

Dehghani, M., Sharpe, L., & Nicholas, M. K. (2004). Modification of attentional biases in chronic pain patients: A preliminary study. *European Journal of Pain*, *8*(6), 585–594. http://doi.org/10.1016/j.ejpain.2004.02.003

Deimling, G. T., Bowman, K. F., Sterns, S., Wagner, L. J., & Kahana, B. (2006). Cancer-related health worries and psychological distress among older adult, long-term cancer survivors. *Psycho-Oncology*, *15*(4), 306–320. http://doi.org/10.1002/pon.955

DeMore, M., & Cohen, L. L. (2005). Distraction for pediatric immunization pain: A critical review. *Journal of Clinical Psychology in Medical Settings*. http://doi.org/10.1007/s10880-005-7813-1

Derryberry, D., & Reed, M. A. (2002). Anxiety-related attentional biases and their regulation by attentional control. *Journal of Abnormal Psychology*, *111*(2), 225–236. http://doi.org/10.1037//0021-843x.111.2.225

Dineen, K. A., & Hadwin, J. A. (2004). Anxious and depressive symptoms and children's judgements of their own and others' interpretation of ambiguous social scenarios. *Journal of Anxiety Disorders*, *18*(4), 499–513. http://doi.org/10.1016/S0887-6185(03)00030-6

Dudeney, J., Sharpe, L., & Hunt, C. (2015). Attentional bias towards threatening stimuli in

children with anxiety: A meta-analysis. *Clinical Psychology Review*. http://doi.org/10.1016/j.cpr.2015.05.007

Duncan, S., & Barrett, L. F. (2007). Affect is a form of cognition: A neurobiological analysis. *Cognition & Emotion*, *21*(6), 1184–1211. http://doi.org/10.1080/02699930701437931

Durnez, W., & Van Damme, S. (2015). Trying to Fix a Painful Problem: The Impact of Pain Control Attempts on the Attentional Prioritization of a Threatened Body Location. *The Journal of Pain*, *16*(2), 135–143. http://doi.org/10.1016/j.jpain.2014.10.012

Eccleston, C., & Crombez, G. (1999). Pain demands attention: a cognitive-affective model of the interruptive function of pain. *Psychological Bulletin*, *125*(3), 356–366. http://doi.org/10.1037/0033-2909.125.3.356

Eccleston, C., & Crombez, G. (2007). Worry and chronic pain: A misdirected problem solving model. *Pain*, *132*, 233–236.

Eccleston, C., Crombez, G., Scotford, A., Clinch, J., & Connell, H. (2004). Adolescent chronic pain: Patterns and predictors of emotional distress in adolescents with chronic pain and their parents. *Pain*, *108*(3), 221–229. http://doi.org/10.1016/j.pain.2003.11.008

Eccleston, C., Fisher, E. A., Vervoort, T., & Crombez, G. (2012). Worry and catastrophizing about pain in youth: A reappraisal. *Pain*, *153*(8), 1560–1562. http://doi.org/10.1016/j.pain.2012.02.039

Edwards, L. C., & Pearce, S. A. (1994). Word completion in chronic pain: evidence for schematic representation of pain? *Journal of Abnormal Psychology*, *103*(2), 379–382. http://doi.org/10.1037/0021-843X.103.2.379

Egger, H. L., & Angold, A. (2006). Common emotional and behavioral disorders in preschool children: Presentation, nosology, and epidemiology. *Journal of Child Psychology and Psychiatry and Allied Disciplines*. http://doi.org/10.1111/j.1469-7610.2006.01618.x

Ekman, P., Friesen, W. V., & Hager, J. C. (2002). *Facial Action Coding System - Investigator's Guide*. *FACS*. http://doi.org/10.1016/j.msea.2004.04.064

Eldar, S., Apter, A., Lotan, D., Edgar, K. P., Naim, R., Fox, N. A., … Bar-Haim, Y. (2012). Attention bias modification treatment for pediatric anxiety disorders: a randomized controlled trial. *The American Journal of Psychiatry*, *169*(2), 213–20. http://doi.org/http://dx.doi.org/10.1176/appi.ajp.2011.11060886

El-Metwally, A., Salminen, J. J., Auvinen, A., Kautiainen, H., & Mikkelsson, M. (2004). Prognosis of non-specific musculoskeletal pain in preadolescents: A prospective 4-year follow-up study till adolescence. *Pain*, *110*(3), 550–559. http://doi.org/10.1016/j.pain.2004.03.021

Eriksen, B. A., & Eriksen, C. W. (1974). Effects of noise letters upon the identification of a target letter in a nonsearch task. *Perception & Psychophysics*, *16*(1), 143–149. http://doi.org/10.3758/BF03203267

Esbjørn, B. H., Sømhovd, M. J., Turnstedt, C., & Reinholdt-Dunne, M. L. (2012). Assessing the revised child anxiety and depression scale (RCADS) in a national sample of Danish youth aged 8-16 years. *PLoS ONE*, *7*(5). http://doi.org/10.1371/journal.pone.0037339

Everaert, J., Duyck, W., & Koster, E. H. W. (2014). Attention, interpretation, and memory biases in subclinical depression: A proof-of-principle test of the combined cognitive biases hypothesis. *Emotion (Washington, D.C.)*, *14*(2), 331–40. http://doi.org/10.1037/a0035250

Everaert, J., Koster, E. H. W., & Derakshan, N. (2012). The combined cognitive bias hypothesis in depression. *Clinical Psychology Review*, *32*(5), 413–424. http://doi.org/10.1016/j.cpr.2012.04.003

Fales, J. L., & Forgeron, P. (2014). The importance of friendships in youth with chronic pain : The next critical wave of research. *Pediatric Pain Letter*, *16*(3).

Fan, J., McCandliss, B. D., Sommer, T., Raz, A., & Posner, M. I. (2002). Testing the

efficiency and independence of attentional networks. *Journal of Cognitive Neuroscience*, *14*(3), 340–347. http://doi.org/10.1162/089892902317361886

Field, A. P., & Lester, K. J. (2010). Is there room for "development" in developmental models of information processing biases to threat in children and adolescents? *Clin Child Fam Psychol Rev*, *13*(4), 315–332. http://doi.org/10.1007/s10567-010-0078-8

Finan, P. H., & Garland, E. L. (2015). The role of positive affect in pain and its treatment. *The Clinical Journal of Pain*, *31*, 177–87. http://doi.org/10.1097/AJP.0000000000000092

Fisher, E., Heathcote, L. C., Palermo, T. M., de C Williams, A. C., Lau, J., & Eccleston, C. (2014). Systematic Review and Meta-analysis: Psychological Therapies for Children with Chronic Pain. *Journal of Pediatric Psychology*, *39*(8), 763–782. http://doi.org/10.1093/jpepsy/jsu008

Fitzgerald, M. (2011). The Neurobiology of Chronic Pain in Children. In B. C. McClain & S. Suresh (Eds.), *Handbook of Pediatric Chronic Pain* (pp. 15–25). Springer.

Forgeron, P. a, King, S., Stinson, J. N., McGrath, P. J., MacDonald, A. J., & Chambers, C. T. (2010). Social functioning and peer relationships in children and adolescents with chronic pain: A systematic review. *Pain Research & Management*, *15*(1), 27–41.

Fox, E., Zougkou, K., Ashwin, C., & Cahill, S. (2015). Investigating the efficacy of attention bias modification in reducing high spider fear: The role of individual differences in initial bias. *Journal of Behavior Therapy and Experimental Psychiatry*, *49*, 84–93. http://doi.org/10.1016/j.jbtep.2015.05.001

Franklin, Z. C., Holmes, P. S., Smith, N. C., & Fowler, N. E. (2016). Personality Type Influences Attentional Bias in Individuals with Chronic Back Pain. *PLoS ONE*, *11*(1). http://doi.org/10.1371/journal.pone.0147035

García-López, L. J., Olivares, J., Hidalgo, M. D., Beidel, D. C., & Turner, S. M. (2001). Psychometric Properties of the Social Phobia and Anxiety Inventory, the Social Anxiety Scale for Adolescents, the Fear of Negative Evaluation Scale, and the Social Avoidance and Distress Scale in an Adolescent Spanish-Speaking Sample. *Journal of Psychopathology and Behavioral Assessment*, *23*(1), 51–59. http://doi.org/10.1023/A:1011043607878

Garcia-Lopez, L. J., Turner, S. M., Beidel, D. C., La Greca, A. M., Olivares, J., & Dolores, H. M. (2002). A pilot study on normative data for two social anxiety measures: The Social Phobia and Anxiety Inventory and the Social Anxiety Scale for Adolescents. *International Journal of Clinical and Health Psychology*, *2*(3), 467–476.

Garcia-Palacios, a, Herrero, R., Belmonte, M. a, Castilla, D., Guixeres, J., Molinari, G., & Banos, R. M. (2014). Ecological momentary assessment for chronic pain in fibromyalgia using a smartphone: a randomized crossover study. *European Journal of Pain (London, England)*, *18*(6), 862–872. http://doi.org/10.1002/j.1532-2149.2013.00425.x

Gatchel, R. J. (1996). Psychological disorders and chronic pain: Cause-and-effect relationships. *Psychological Approaches to Pain Management: A Practitioner's Handbook*, 33–52. Retrieved from Guilford Press\nUS.\nhttp://ovidsp.ovid.com/ovidweb.cgi?T=JS&CSC=Y&NEWS=N&PAGE=fulltext&D=psyc3&AN=1996-97724-002\nhttp://nhs5195535.resolver.library.nhs.uk/?sid=OVID:psycdb&id=pmid:&id=doi:&issn=&isbn=0898622921&volume=&issue=&spage=33&pages=33-52&date=1

George, S. Z., Dannecker, E. A., & Robinson, M. E. (2006). Fear of pain, not pain catastrophizing, predicts acute pain intensity, but neither factor predicts tolerance or blood pressure reactivity: An experimental investigation in pain-free individuals. *European Journal of Pain*, *10*(5), 457–465. http://doi.org/10.1016/j.ejpain.2005.06.007

Glare, P. A., Davies, P. S., Finlay, E., Gulati, A., Lemanne, D., Moryl, N., … Syrjala, K. L.

(2014). Pain in Cancer Survivors. *Journal of Clinical Oncology : Official Journal of the American Society of Clinical Oncology*, *32*(16), 1739–1747. http://doi.org/10.1200/JCO.2013.52.4629

Goubert, L., Crombez, G., & Van Damme, S. (2004). The role of neuroticism, pain catastrophizing and pain-related fear in vigilance to pain: A structural equations approach. *Pain*, *107*(3), 234–241. http://doi.org/10.1016/j.pain.2003.11.005

Goubert, L., Vlaeyen, J. W. S., Crombez, G., & Craig, K. D. (2011). Learning about pain from others: An observational learning account. *Journal of Pain*, *12*(2), 167–174. http://doi.org/10.1016/j.jpain.2010.10.001

Grey, S., & Mathews, a. (2000). Effects of training on interpretation of emotional ambiguity. *The Quarterly Journal of Experimental Psychology. A, Human Experimental Psychology*, *53*(4), 1143–1162. http://doi.org/10.1080/713755937

Groenewald, C. B., Essner, B. S., Wright, D., Fesinmeyer, M. D., & Palermo, T. M. (2014). The economic costs of chronic pain among a cohort of treatment seeking adolescents in the United States. *The Journal of Pain : Official Journal of the American Pain Society*, *15*(9), 925–933. http://doi.org/10.1016/j.jpain.2014.06.002

Gupta, S. K. (2011). Intention-to-treat concept: A review. *Perspectives in Clinical Research*, *2*(3), 109–112. http://doi.org/10.4103/2229-3485.83221

Hadwin, J. a., Garner, M., & Perez-Olivas, G. (2006). The development of information processing biases in childhood anxiety: A review and exploration of its origins in parenting. *Clinical Psychology Review*, *26*(7), 876–894. http://doi.org/10.1016/j.cpr.2005.09.004

Hadwin, J., Frost, S., French, C. C., & Richards, a. (1997). Cognitive processing and trait anxiety in typically developing children: evidence for an interpretation bias. *Journal of Abnormal Psychology*, *106*(3), 486–490.

Hakamata, Y., Lissek, S., Bar-Haim, Y., Britton, J. C., Fox, N. A., Leibenluft, E., … Pine, D. S. (2010). Attention bias modification treatment: A meta-analysis toward the establishment of novel treatment for anxiety. *Biological Psychiatry*, *68*(11), 982–990. http://doi.org/10.1016/j.biopsych.2010.07.021

Hall, D. L., Mishel, M. H., & Germino, B. B. (2014). Living with cancer-related uncertainty: Associations with fatigue, insomnia, and affect in younger breast cancer survivors. *Supportive Care in Cancer*, *22*(9), 2489–2495. http://doi.org/10.1007/s00520-014-2243-y

Hanssen, M. M., Peters, M. L., Vlaeyen, J. W. S., Meevissen, Y. M. C., & Vancleef, L. M. G. (2013). Optimism lowers pain: Evidence of the causal status and underlying mechanisms. *Pain*, *154*(1), 53–58. http://doi.org/10.1016/j.pain.2012.08.006

Hayes, A. (2013). Introduction to mediation, moderation, and conditional process analysis. *New York, NY: Guilford*, 3–4. http://doi.org/978-1-60918-230-4

He, C. H., Yu, F., Jiang, Z. C., Wang, J. Y., & Luo, F. (2014). Fearful thinking predicts hypervigilance towards pain-related stimuli in patients with chronic pain. *PsyCh Journal*, *3*(3), 189–200. http://doi.org/10.1002/pchj.57

Heathcote, L. C., Koopmans, M., Eccleston, C., Fox, E., Jacobs, K., Wilkinson, N., & Lau, J. Y. F. (2016). Negative interpretation bias and the experience of pain in adolescents. *The Journal of Pain*, *17*(9), 972–981. http://doi.org/10.1016/j.jpain.2016.05.009

Heathcote, L. C., Lau, J. Y. F., Mueller, S. C., Eccleston, C., Fox, E., Bosmans, M., & Vervoort, T. (2016). Child attention to pain and pain tolerance are dependent upon anxiety and attention control: An eye-tracking study. *European Journal of Pain*. http://doi.org/10.1002/ejp.920

Heathcote, L. C., Vervoort, T., Eccleston, C., Fox, E., Jacobs, K., Van Ryckeghem, D. M. L., & Lau, J. Y. F. (2015). The relationship between adolescents' pain catastrophizing and

attention bias to pain faces is moderated by attention control. *PAIN*, *156*(7), 1334–1341. http://doi.org/10.1097/j.pain.0000000000000174

Heeren, A., De Raedt, R., Koster, E. H. W., & Philippot, P. (2013). The (neuro)cognitive mechanisms behind attention bias modification in anxiety: proposals based on theoretical accounts of attentional bias. *Frontiers in Human Neuroscience*, *7*(April), 119. http://doi.org/10.3389/fnhum.2013.00119

Helzer, E. G., Connor-Smith, J. K., & Reed, M. a. (2009). Traits, states, and attentional gates: temperament and threat relevance as predictors of attentional bias to social threat. *Anxiety, Stress, and Coping*, *22*(1), 57–76. http://doi.org/10.1080/10615800802272244

Hermann, C., Zohsel, K., Hohmeister, J., & Flor, H. (2008). Cortical correlates of an attentional bias to painful and innocuous somatic stimuli in children with recurrent abdominal pain. *Pain*, *136*(3), 397–406. http://doi.org/10.1016/j.pain.2008.01.007

Heyneman, N. E., Fremouw, W. J., Gano, D., Kirkland, F., & Heiden, L. (1990). Individual differences and the effectiveness of different coping strategies for pain. *Cognitive Therapy and Research*, *14*(1), 63–77. http://doi.org/10.1007/BF01173525

Hirsch, C. R., Clark, D. M., & Mathews, A. (2006). Imagery and Interpretations in Social Phobia: Support for the Combined Cognitive Biases Hypothesis. *Behavior Therapy*, *37*(3), 223–236. http://doi.org/10.1016/j.beth.2006.02.001

Holmbeck, G. N. (2002). Post-hoc probing of significant moderational and mediational effects in studies of pediatric populations. *Journal of Pediatric Psychology*, *27*(1), 87–96. http://doi.org/10.1093/jpepsy/27.1.87

Holt-Lunstad, J., Smith, T. B., & Layton, J. B. (2010). Social relationships and mortality risk: A meta-analytic review. *PLoS Medicine*, *7*(7). http://doi.org/10.1371/journal.pmed.1000316

Horn, M. E., Alappattu, M. J., Gay, C. W., & Bishop, M. (2014). Fear of severe pain mediates sex differences in pain sensitivity responses to thermal stimuli. *Pain Research and Treatment*, *2014*. http://doi.org/10.1155/2014/897953

Hotopf, M., Carr, S., Mayou, R., Wadsworth, M., & Wessely, S. (1998). Why do children have chronic abdominal pain, and what happens to them when they grow up? Population based cohort study. *BMJ*, *316*(7139), 1196–1200. http://doi.org/10.1136/bmj.316.7139.1196

Hou, R., Moss-Morris, R., Risdale, A., Lynch, J., Jeevaratnam, P., Bradley, B. P., & Mogg, K. (2014). Attention processes in chronic fatigue syndrome: Attentional bias for health-related threat and the role of attentional control. *Behaviour Research and Therapy*, *52*(1), 9–16. http://doi.org/10.1016/j.brat.2013.10.005

Huber, C., Kunz, M., Artelt, C., & Lautenbacher, S. (2010). Attentional and emotional mechanisms of pain processing and their related factors: A structural equations approach. *Pain Research and Management*, *15*(4), 229–237.

Hudson, M. M., Mertens, A. C., Yasui, Y., Hobbie, W., Chen, H., Gurney, J. G., … Oeffinger, K. C. (2003). Health status of adult long-term survivors of childhood cancer: a report from the Childhood Cancer Survivor Study. *JAMA : The Journal of the American Medical Association*, *290*(12), 1583–1592. http://doi.org/10.1001/jama.290.12.1583

Huguet, A., & Miró, J. (2008). The severity of chronic pediatric pain: an epidemiological study. *The Journal of Pain : Official Journal of the American Pain Society*, *9*(3), 226–236. http://doi.org/10.1016/j.jpain.2007.10.015

Hutton, S. B., & Ettinger, U. (2006). The antisaccade task as a research tool in psychopathology: A critical review. *Psychophysiology*. http://doi.org/10.1111/j.1469-8986.2006.00403.x

Johannes, C. B., Le, T. K., Zhou, X., Johnston, J. A., & Dworkin, R. H. (2010). The

Prevalence of Chronic Pain in United States Adults: Results of an Internet-Based Survey. *Journal of Pain*, *11*(11), 1230–1239. http://doi.org/10.1016/j.jpain.2010.07.002

Jones, E. B., & Sharpe, L. (2014). The effect of cognitive bias modification for interpretation on avoidance of pain during an acute experimental pain task. *Pain*, *155*(8), 1569–1576. http://doi.org/10.1016/j.pain.2014.05.003

Karsdorp, P. A., Ranson, S., Schrooten, M. G. S., & Vlaeyen, J. W. S. (2012). Pain catastrophizing, threat, and the informational value of mood: Task persistence during a painful finger pressing task. *Pain*, *153*(7), 1410–1417. http://doi.org/http://dx.doi.org/10.1016/j.pain.2012.02.026

Kashikar-Zuck, S., Flowers, S. R., Claar, R. L., Guite, J. W., Logan, D. E., Lynch-Jordan, A. M., … Wilson, A. C. (2011). Clinical utility and validity of the Functional Disability Inventory (FDI) among a multicenter sample of youth with chronic pain. *Pain*, *152*(7), 1600–1607. http://doi.org/10.1016/j.pain.2011.02.050

Kashikar-Zuck, S., Parkins, I. S., Ting, T. V., Verkamp, E., Lynch-Jordan, A., Passo, M., & Graham, T. B. (2010). Controlled follow-up study of physical and psychosocial functioning of adolescents with juvenile primary fibromyalgia syndrome. *Rheumatology*, *49*(11), 2204–2209. http://doi.org/10.1093/rheumatology/keq254

Keogh, E., & Cochrane, M. (2002). Anxiety sensitivity, cognitive biases, and the experience of pain. *The Journal of Pain : Official Journal of the American Pain Society*, *3*(4), 320–329. http://doi.org/10.1054/jpai.2002.125182

Keogh, E., & Eccleston, C. (2006). Sex differences in adolescent chronic pain and pain-related coping. *Pain*, *123*(3), 275–284. http://doi.org/10.1016/j.pain.2006.03.004

Keogh, E., Ellery, D., Hunt, C., & Hannent, I. (2001). Selective attentional bias for pain-related stimuli amongst pain fearful individuals. *Pain*, *91*(1-2), 91–100. http://doi.org/10.1016/S0304-3959(00)00422-X

Keogh, E., Hamid, R., Hamid, S., & Ellery, D. (2004). Investigating the effect of anxiety sensitivity, gender and negative interpretative bias on the perception of chest pain. *Pain*, *111*(1-2), 209–217. http://doi.org/10.1016/j.pain.2004.06.017

Khatibi, A., Dehghani, M., Sharpe, L., Asmundson, G. J. G., & Pouretemad, H. (2009). Selective attention towards painful faces among chronic pain patients: Evidence from a modified version of the dot-probe. *Pain*, *142*(1-2), 42–47. http://doi.org/10.1016/j.pain.2008.11.020

Khatibi, A., Schrooten, M. G. S., Vancleef, L. M. G., & Vlaeyen, J. W. S. (2014). An experimental examination of catastrophizing-related interpretation bias for ambiguous facial expressions of pain using an incidental learning task. *Frontiers in Psychology*, *5*(September), 1–10. http://doi.org/10.3389/fpsyg.2014.01002

Khatibi, A., Sharpe, L., Jafari, H., Gholami, S., & Dehghani, M. (2015). Interpretation biases in chronic pain patients: an incidental learning task. *European Journal of Pain*, *19*(8), 1139–1147. http://doi.org/10.1002/ejp.637

Kindt, M., Bierman, D., & Brosschot, J. F. (1997). Cognitive bias in spider fear and control children: assessment of emotional interference by a card format and a single-trial format of the stroop task. *Journal of Experimental Child Psychology*, *66*(2), 163–179. http://doi.org/10.1006/jecp.1997.2376

Kindt, M., & Van Den Hout, M. (2001). Selective attention and anxiety: A perspective on developmental issues and the causal status. *Journal of Psychopathology and Behavioral Assessment*, *23*(3), 193–202. http://doi.org/10.1023/a:1010921405496

King, S., Chambers, C. T., Huguet, A., MacNevin, R. C., McGrath, P. J., Parker, L., & MacDonald, A. J. (2011). The epidemiology of chronic pain in children and adolescents revisited: A systematic review. *Pain*, *152*(12), 2729–2738. http://doi.org/10.1016/j.pain.2011.07.016

Kleiber, C., & Harper, D. (1999). Effects of Distraction on Children's Pain and Distress During Medical Procedures: A Meta-Analysis. *Nursing Research*, *48*, 44–49.

Knook, L. M. E., Konijnenberg, A. Y., Van Der Hoeven, J., Kimpen, J. L. L., Buitelaar, J. K., Van Engeland, H., & De Graeff-Meeder, E. R. (2011). Psychiatric disorders in children and adolescents presenting with unexplained chronic pain: What is the prevalence and clinical relevancy? *European Child and Adolescent Psychiatry*, *20*(1), 39–48. http://doi.org/10.1007/s00787-010-0146-0

Komogortsev, O. V., Gobert, D. V., Jayarathna, S., Koh, D. H., & Gowda, S. M. (2010). Standardization of automated analyses of oculomotor fixation and saccadic behaviors. *IEEE Transactions on Biomedical Engineering*, *57*(11), 2635–2645. http://doi.org/10.1109/TBME.2010.2057429

Koster, E. H. W., Crombez, G., Verschuere, B., & De Houwer, J. (2004). Selective attention to threat in the dot probe paradigm: Differentiating vigilance and difficulty to disengage. *Behaviour Research and Therapy*, *42*(10), 1183–1192. http://doi.org/10.1016/j.brat.2003.08.001

Koster, E. H. W., De Lissnyder, E., & De Raedt, R. (2013). Rumination is characterized by valence-specific impairments in switching of attention. *Acta Psychologica*, *144*(3), 563–570. http://doi.org/10.1016/j.actpsy.2013.09.008

Koutantji, M., Pearce, S. a., Oakley, D. a., & Feinmann, C. (1999). Children in pain: An investigation of selective memory for pain and psychological adjustment. *Pain*, *81*(3), 237–244. http://doi.org/10.1016/S0304-3959(99)00020-2

La Greca, A. M., & Lopez, N. (1998). Social Anxiety among Adolescents: Linkages with peer relations and friendships. *Journal of Abnormal Child Psychology*, *26*(2), 83–94. http://doi.org/10.1023/A:1022684520514

Lau, J. Y. F. (2013). Cognitive bias modification of interpretations: A viable treatment for child and adolescent anxiety? *Behaviour Research and Therapy*, *51*(10), 614–622. http://doi.org/10.1016/j.brat.2013.07.001

Lautenbacher, S., Huber, C., Kunz, M., Parthum, A., Weber, P. G., Griessinger, N., & Sittl, R. (2009). Hypervigilance as predictor of postoperative acute pain: its predictive potency compared with experimental pain sensitivity, cortisol reactivity, and affective state. *The Clinical Journal of Pain*, *25*(2), 92–100. http://doi.org/10.1097/AJP.0b013e3181850dce

Lautenbacher, S., Huber, C., Schöfer, D., Kunz, M., Parthum, A., Weber, P. G., … Sittl, R. (2010). Attentional and emotional mechanisms related to pain as predictors of chronic postoperative pain: A comparison with other psychological and physiological predictors. *Pain*, *151*(3), 722–731. http://doi.org/10.1016/j.pain.2010.08.041

Lee-Jones, C., Humphris, G., Dixon, R., & Hatcher, M. B. (1997). Fear of cancer recurrence - A literature review and proposed cognitive formulation to explain exacerbation of recurrence fears. *Psycho-Oncology*, *6*(2), 95–105. http://doi.org/10.1002/(SICI)1099-1611(199706)6:2<95::AID-PON250>3.0.CO;2-B

Leeuw, M., Goossens, M. E. J. B., Linton, S. J., Crombez, G., Boersma, K., & Vlaeyen, J. W. S. (2007). The fear-avoidance model of musculoskeletal pain: Current state of scientific evidence. *Journal of Behavioral Medicine*, *30*(1), 77–94. http://doi.org/10.1007/s10865-006-9085-0

Lester, K. J., Seal, K., Nightingale, Z. C., & Field, A. P. (2010). Are children's own interpretations of ambiguous situations based on how they perceive their mothers have interpreted ambiguous situations for them in the past? *Journal of Anxiety Disorders*, *24*(1), 102–8. http://doi.org/10.1016/j.janxdis.2009.09.004

Levy, M. H., Chwistek, M., & Mehta, R. S. (2008). Management of chronic pain in cancer survivors. *Cancer Journal (Sudbury, Mass.)*, *14*(6), 401–409.

http://doi.org/10.1097/PPO.0b013e31818f5aa7
Lipsitz, J. D., Masia, C., Apfel, H., Marans, Z., Gur, M., Dent, H., & Fyer, A. J. (2005). Noncardiac chest pain and psychopathology in children and adolescents. *Journal of Psychosomatic Research*, *59*(3), 185–188. http://doi.org/10.1016/j.jpsychores.2005.05.004
MacLeod, C. (2012). Cognitive bias modification procedures in the management of mental disorders. *Current Opinion in Psychiatry*, *25*(2), 114–120. http://doi.org/10.1097/YCO.0b013e32834fda4a
MacLeod, C., Mathews, A., & Tata, P. (1986). Attentional bias in emotional disorders. *Journal of Abnormal Psychology*, *95*(1), 15–20. http://doi.org/10.1037/0021-843X.95.1.15
MacLeod, C., Soong, L. Y., Rutherford, E. M., & Campbell, L. W. (2007). Internet-delivered assessment and manipulation of anxiety-linked attentional bias: validation of a free-access attentional probe software package. *Behavior Research Methods*, *39*(3), 533–538. http://doi.org/10.3758/BF03193023
Macmillan Cancer Support. (n.d.). What to do after treatment. Retrieved June 20, 2004, from http://www.macmillan.org.uk/documents/cancerinfo/livingwithandaftercancer/whattodoaftertreatment.pdf
Martin, A. L., McGrath, P. A., Brown, S. C., & Katz, J. (2007). Children with chronic pain: Impact of sex and age on long-term outcomes. *Pain*, *128*(1-2), 13–19. http://doi.org/10.1016/j.pain.2006.08.027
Mathews, A., & Mackintosh, B. (1998). A cognitive model of selective processing in anxiety. *Cognitive Therapy and Research*. http://doi.org/10.1023/A:1018738019346
Mathews, A., & MacLeod, C. (2005). Cognitive vulnerability to emotional disorders. *Annual Review of Clinical Psychology*, *1*, 167–195. http://doi.org/10.1146/annurev.clinpsy.1.102803.143916
Mathews, A., Yiend, J., & Lawrence, A. D. (2004). Individual differences in the modulation of fear-related brain activation by attentional control. *Journal of Cognitive Neuroscience*, *16*(10), 1683–94. http://doi.org/10.1162/0898929042947810
Mathyssek, C. M., Olino, T. M., Hartman, C. A., Ormel, J., Verhulst, F. C., & Van Oort, F. V. A. (2013). Does the Revised Child Anxiety and Depression Scale (RCADS) measure anxiety symptoms consistently across adolescence? The TRAILS study. *International Journal of Methods in Psychiatric Research*, *22*(1), 27–35. http://doi.org/10.1002/mpr.1380
McGowan, N., Sharpe, L., Refshauge, K., & Nicholas, M. K. (2009). The effect of attentional re-training and threat expectancy in response to acute pain. *Pain*, *142*(1-2), 101–107. http://doi.org/10.1016/j.pain.2008.12.009
McGrath, P. J., Latimer, M., Finley, G. A., & Chambers, C. T. (2009). Measurement of pain in children. *Pain Research and Management*, *14*(1), 11. http://doi.org/10.1097/00000542-200203000-00002
McKellar, J. D., Clark, M. E., & Shriner, J. (2003). The cognitive specificity of associative responses in patients with chronic pain. *The British Journal of Clinical Psychology / the British Psychological Society*, *42*(Pt 1), 27–39. http://doi.org/10.1348/014466503762841995
Meesters, C., Muris, P., & Van Rooijen, B. (2007). Relations of neuroticism and attentional control with symptoms of anxiety and aggression in non-clinical children. *Journal of Psychopathology and Behavioral Assessment*, *29*(3), 149–158. http://doi.org/10.1007/s10862-006-9037-6
Mehnert, A., & Koch, U. (2008). Psychological comorbidity and health-related quality of life and its association with awareness, utilization, and need for psychosocial support in a

cancer register-based sample of long-term breast cancer survivors. *Journal of Psychosomatic Research*, *64*(4), 383–391. http://doi.org/10.1016/j.jpsychores.2007.12.005

Merskey, H., & Bogduk, N. (1994). IASP Task Force on Taxonomy Part III: Pain Terms, A Current List with Definitions and Notes on Usage. http://doi.org/http://dx.doi.org/10.1016/0304-3959(86)90113-2

Miers, A. C., Blöte, A. W., Bögels, S. M., & Westenberg, P. M. (2008). Interpretation bias and social anxiety in adolescents. *Journal of Anxiety Disorders*, *22*(8), 1462–1471. http://doi.org/10.1016/j.janxdis.2008.02.010

Mogg, K., & Bradley, B. P. (1998). A cognitive-motivational analysis of anxiety. *Behaviour Research and Therapy*. http://doi.org/10.1016/S0005-7967(98)00063-1

Mogg, K., Mathews, A., & Weinman, J. (1987). Memory bias in clinical anxiety. *Journal of Abnormal Psychology*, *96*(2), 94–98. http://doi.org/10.1037/0021-843X.96.2.94

Monk, C. S., McClure, E. B., Nelson, E. E., Zarahn, E., Bilder, R. M., Leibenluft, E., … Pine, D. S. (2003). Adolescent immaturity in attention-related brain engagement to emotional facial expressions. *NeuroImage*, *20*(1), 420–428. http://doi.org/10.1016/S1053-8119(03)00355-0

Moore, D. J., Keogh, E., & Eccleston, C. (2012). The interruptive effect of pain on attention The interruptive effect of pain on attention. *The Quarterly Journal of Experimental Psychology. A, Human Experimental Psychology*, *65*(3), 565–586.

Moretti, M. M., & Peled, M. (2004). Adolescent-parent attachment: Bonds that support healthy development. *Paediatrics and Child Health*.

Moseley, G. L. (2007). Reconceptualising pain according to modern pain science. *Physical Therapy Reviews*, *12*(3), 169–178. http://doi.org/10.1179/108331907X223010

Moskowitz, D. S., & Young, S. N. (2006). Ecological momentary assessment: what it is and why it is a method of the future in clinical psychopharmacology. *Journal of Psychiatry & Neuroscience : JPN*, *31*(1), 13–20. Retrieved from /pmc/articles/PMC1325062/?report=abstract

Munafò, M. R., & Stevenson, J. (2003). Selective processing of threat-related cues in day surgery patients and prediction of post-operative pain. *British Journal of Health Psychology*, *8*(Pt 4), 439–449. http://doi.org/10.1348/135910703770238293

Muris, P., de Jong, P. J., & Engelen, S. (2004). Relationships between neuroticism, attentional control, and anxiety disorders symptoms in non-clinical children. *Personality and Individual Differences*, *37*(4), 789–797. http://doi.org/10.1016/j.paid.2003.10.007

Muris, P., Meesters, C., Van Den Hout, A., Wessels, S., Franken, I., & Rassin, E. (2007). Personality and temperament correlates of pain catastrophizing in young adolescents. *Child Psychiatry and Human Development*, *38*(3), 171–181. http://doi.org/10.1007/s10578-007-0054-9

Muris, P., Van Der Pennen, E., Sigmond, R., & Mayer, B. (2008). Symptoms of anxiety, depression, and aggression in non-clinical children: Relationships with self-report and performance-based measures of attention and effortful control. *Child Psychiatry and Human Development*, *39*(4), 455–467. http://doi.org/10.1007/s10578-008-0101-1

National Cancer Intelligence Network. (2012). *National Registry of Childhood Tumours Progress Report , 2012*.

Nelson, C. A., Bloom, F. E., Cameron, J. L., Amaral, D., Dahl, R. E., & Pine, D. (2002). An integrative, multidisciplinary approach to the study of brain-behavior relations in the context of typical and atypical development. *Development and Psychopathology*, *14*(3), 499–520. http://doi.org/10.1017/S0954579402003061

Nelson, E. E., Leibenluft, E., McClure, E. B., & Pine, D. S. (2005). The social re-orientation of adolescence: a neuroscience perspective on the process and its relation to

psychopathology. *Psychological Medicine*, *35*, 163–174. http://doi.org/10.1017/S0033291704003915

Niederstrasser, N. G., Maxwell Slepian, P., Mankovsky-Arnold, T., Lariviére, C., Vlaeyen, J. W., & Sullivanz, M. J. L. (2014). An experimental approach to examining psychological contributions to multisite musculoskeletal pain. *Journal of Pain*, *15*(11), 1156–1165. http://doi.org/10.1016/j.jpain.2014.08.007

Noel, M., Chambers, C. T., McGrath, P. J., Klein, R. M., & Stewart, S. H. (2012). The influence of children's pain memories on subsequent pain experience. *Pain*, *153*(8), 1563–1572. http://doi.org/10.1016/j.pain.2012.02.020

Noel, M., Chambers, C. T., Petter, M., McGrath, P. J., Klein, R. M., & Stewart, S. H. (2012). Pain is not over when the needle ends: a review and preliminary model of acute pain memory development in childhood. *Pain Management*, *2*(5), 487–497. http://doi.org/10.2217/pmt.12.41

Noel, M., Ms, C., Chambers, C. T., Mcgrath, P. J., Klein, R. M., & Stewart, S. H. (2012). The Role of State Anxiety in Children ' s Memories for Pain, *37*(5), 567–579.

Noel, M., Palermo, T. M., Chambers, C. T., Taddio, A., & Hermann, C. (2015). Remembering the pain of childhood : applying a developmental perspective to the study of pain memories, *156*(1).

Noel, M., Rabbitts, J. A., Tai, G. G., & Palermo, T. M. (2015). Remembering pain after surgery: a longitudinal examination of the role of pain catastrophizing in children's and parents' recall. *Pain*, *156*(5), 800–8. http://doi.org/10.1097/j.pain.0000000000000102

Notebaert, L., Crombez, G., Vogt, J., De Houwer, J., Van Damme, S., & Theeuwes, J. (2011). Attempts to control pain prioritize attention towards signals of pain: An experimental study. *Pain*, *152*(5), 1068–1073. http://doi.org/10.1016/j.pain.2011.01.020

Olejnik, S., & Algina, J. (2000). Measures of Effect Size for Comparative Studies: Applications, Interpretations, and Limitations. *Contemporary Educational Psychology*, *25*(3), 241–286. http://doi.org/10.1006/ceps.2000.1040

Olthuis, J. V., Stewart, S. H., Watt, M. C., Sabourin, B. C., & Keogh, E. (2012). Anxiety sensitivity and negative interpretation biases: Their shared and unique associations with anxiety symptoms. *Journal of Psychopathology and Behavioral Assessment*, *34*(3), 332–342. http://doi.org/10.1007/s10862-012-9286-5

Orchard, F., Pass, L., & Reynolds, S. (2016a). `It Was All My Fault'; Negative Interpretation Bias in Depressed Adolescents. *Journal of Abnormal Child Psychology*, *44*(5), 991–998. http://doi.org/10.1007/s10802-015-0092-x

Orchard, F., Pass, L., & Reynolds, S. (2016b). Associations Between Interpretation Bias and Depression in Adolescents. *Cognitive Therapy and Research*, *40*(4), 577–583. http://doi.org/10.1007/s10608-016-9760-6

Owens, M., Koster, E. H. W., & Derakshan, N. (2013). Improving attention control in dysphoria through cognitive training: Transfer effects on working memory capacity and filtering efficiency. *Psychophysiology*, *50*(3), 297–307. http://doi.org/10.1111/psyp.12010

Oxford English Dictionary. (2014). Oxford English Dictionary Online.

Palermo, T. M. (2000). Impact of recurrent and chronic pain on child and family daily functioning: a critical review of the literature. *Journal of Developmental and Behavioral Pediatrics : JDBP*, *21*, 58–69. http://doi.org/10.1097/00004703-200002000-00011

Palermo, T. M., Valrie, C. R., & Karlson, C. W. (2014). Family and parent influences on pediatric chronic pain: a developmental perspective. *The American Psychologist*, *69*(2), 142–52. http://doi.org/10.1037/a0035216

Parmelee, P. a, Katz, I. R., & Lawton, M. P. (1991). The relation of pain to depression among institutionalized aged. *Journal of Gerontology*, *46*(1), P15–P21.

Parry, C. (2003). Embracing uncertainty: an exploration of the experiences of childhood cancer survivors. *Qualitative Health Research*, *13*(2), 227–246. http://doi.org/10.1177/1049732302239600

Pennebaker, J. W. (1982). *The Psychology of Physical Symptoms*. New York: Springer-Verlag.

Pennebaker, J. W. (2000). Psychological factors influencing the reporting of physical symptoms. In *The Science of Self-Report: Implications for research and practice* (pp. 299–315).

Perneger, T. V. (1998). What's wrong with Bonferroni adjustments. *BMJ (Clinical Research Ed.)*, *316*(7139), 1236–1238. http://doi.org/10.1136/bmj.316.7139.1236

Perquin, C. W., Hazebroek-Kampschreur, A. a J. M., Hunfeld, J. a M., Bohnen, A. M., Van Suijlekom-Smit, L. W. a, Passchier, J., & Van Der Wouden, J. C. (2000). Pain in children and adolescents: A common experience. *Pain*, *87*(1), 51–58. http://doi.org/10.1016/S0304-3959(00)00269-4

Peters, M. L. (2015). Emotional and cognitive influences on pain experience. *Modern Trends in Pharmacopsychiatry*, *30*, 138–152. http://doi.org/10.1159/000435938

Peters, M. L., Vlaeyen, J. W. S., & Kunnen, A. M. W. (2002). Is pain-related fear a predictor of somatosensory hypervigilance in chronic low back pain patients? *Behaviour Research and Therapy*, *40*(1), 85–103. http://doi.org/10.1016/S0005-7967(01)00005-5

Peters, M. L., Vlaeyen, J. W. S., & Weber, W. E. J. (2005). The joint contribution of physical pathology, pain-related fear and catastrophizing to chronic back pain disability. *Pain*, *113*(1-2), 45–50. http://doi.org/10.1016/j.pain.2004.09.033

Petter, M., McGrath, P. J., Chambers, C. T., & Dick, B. D. (2014). The effects of mindful attention and state mindfulness on acute experimental pain among adolescents. *Journal of Pediatric Psychology*, *39*(5), 521–531. http://doi.org/10.1093/jpepsy/jsu007

Peuckmann, V., Ekholm, O., Rasmussen, N. K., Groenvold, M., Christiansen, P., Moller, S., … Sjogren, P. (2009). Chronic pain and other sequelae in long-term breast cancer survivors: Nationwide survey in Denmark. *European Journal of Pain*, *13*(5), 478–485. http://doi.org/10.1016/j.ejpain.2008.05.015

Pincus, T., & Morley, S. (2001). Cognitive-processing bias in chronic pain: A review and integration. *Psychological Bulletin*, *127*(5), 599–617. http://doi.org/10.1037//0033-2909.127.5.599

Pincus, T., Pearce, S., McClelland, A., Farley, S., & Vogel, S. (1994). Interpretation bias in responses to ambiguous cues in pain patients. *Journal of Psychosomatic Research*, *38*(4), 347–353. http://doi.org/10.1016/0022-3999(94)90039-6

Pincus, T., Pearce, S., McClelland, A., & Isenberg, D. (1995). Endorsement and memory bias of self-referential pain stimuli in depressed pain patients. *The British Journal of Clinical Psychology / the British Psychological Society*, *34 (Pt 2)*, 267–277. http://doi.org/10.1111/j.2044-8260.1995.tb01461.x

Pincus, T., Pearce, S., & Perrott, A. (1996). Pain patients' bias in the interpretation of ambiguous homophones. *The British Journal of Medical Psychology*, *69*, 259–266. http://doi.org/10.1111/j.2044-8341.1996.tb01868.x

Platt, B., Waters, A. M., Schulte-Koerne, G., Engelmann, L., & Salemink, E. (2016). A review of cognitive biases in youth depression: attention, interpretation and memory. *Cognition and Emotion*, *9931*, 1–22. http://doi.org/10.1080/02699931.2015.1127215

Preacher, K. J., & Kelley, K. (2011). Effect size measures for mediation models: quantitative strategies for communicating indirect effects. *Psychological Methods*, *16*(2), 93–115. http://doi.org/10.1037/a0022658

Quaresma, M., Coleman, M. P., & Rachet, B. (2015). 40-year trends in an index of survival for all cancers combined and survival adjusted for age and sex for each cancer in

England and Wales, 1971–2011: a population-based study. *The Lancet*, *385*(9974), 1206–1218. http://doi.org/http://dx.doi.org/10.1016/S0140-6736(14)61396-9

Quartana, P. J., Campbell, C. M., & Edwards, R. R. (2009). Pain catastrophizing : a critical review. *Expert Rev Neurother*, *9*(5), 745–758. http://doi.org/10.1586/ERN.09.34.Pain

Rabbitts, J. A., Groenewald, C. B., Tai, G. G., & Palermo, T. M. (2014). Presurgical psychosocial predictors of acute postsurgical pain and quality of life in children undergoing major surgery. *The Journal of Pain : Official Journal of the American Pain Society*, *16*(3), 226–234. http://doi.org/10.1016/j.jpain.2014.11.015

Remmerswaal, D., Muris, P., & Huijding, J. (2015). Transmission of Cognitive Bias and Fear From Parents to Children: An Experimental Study. *Journal of Clinical Child & Adolescent Psychology*, (February), 1–13. http://doi.org/10.1080/15374416.2014.987378

Robinson, M. E., Bialosky, J. E., Bishop, M. D., Price, D. D., & George, S. Z. (2010). Supra-threshold scaling, temporal summation, and after-sensation: Relationships to each other and anxiety/fear. *Journal of Pain Research*, *3*, 25–32. http://doi.org/10.2147/JPR.S9462

Roelofs, J., Peters, M. L., van der Zijden, M., Thielen, F. G. J. M., & Vlaeyen, J. W. S. (2003). Selective attention and avoidance of pain-related stimuli: a dot-probe evaluation in a pain-free population. *The Journal of Pain*, *4*(6), 322–328. http://doi.org/http://dx.doi.org/10.1016/S1526-5900(03)00634-5

Roelofs, J., Peters, M. L., Zeegers, M. P. A., & Vlaeyen, J. W. S. (2002). The modified Stroop paradigm as a measure of selective attention towards pain-related stimuli among chronic pain patients: a meta-analysis. *European Journal of Pain (London, England)*, *6*(4), 273–81. http://doi.org/10.1053/eujp.2002.0337

Rommelse, N. N. J., Van der Stigchel, S., & Sergeant, J. A. (2008). A review on eye movement studies in childhood and adolescent psychiatry. *Brain and Cognition*, *68*(3), 391–414. http://doi.org/10.1016/j.bandc.2008.08.025

Rueda, M. R., Fan, J., McCandliss, B. D., Halparin, J. D., Gruber, D. B., Lercari, L. P., & Posner, M. I. (2004). Development of attentional networks in childhood. *Neuropsychologia*, *42*(8), 1029–1040. http://doi.org/10.1016/j.neuropsychologia.2003.12.012

Rueda, M. R., Rothbart, M. K., McCandliss, B. D., Saccomanno, L., & Posner, M. I. (2005). Training, maturation, and genetic influences on the development of executive attention. *Proceedings of the National Academy of Sciences of the United States of America*, *102*(41), 14931–6. http://doi.org/10.1073/pnas.0506897102

Rusu, A. C., Pincus, T., & Morley, S. (2012). Depressed pain patients differ from other depressed groups: Examination of cognitive content in a sentence completion task. *Pain*, *153*(9), 1898–1904. http://doi.org/10.1016/j.pain.2012.05.034

Salemink, E., van den Hout, M. a., & Kindt, M. (2007). Selective attention and threat: Quick orienting versus slow disengagement and two versions of the dot probe task. *Behaviour Research and Therapy*, *45*(3), 607–615. http://doi.org/10.1016/j.brat.2006.04.004

Salemink, E., & Wiers, R. W. (2012). Adolescent threat-related interpretive bias and its modification: The moderating role of regulatory control. *Behaviour Research and Therapy*, *50*(1), 40–46. http://doi.org/10.1016/j.brat.2011.10.006

Salvucci, D. D., Salvucci, D. D., Goldberg, J. H., & Goldberg, J. H. (2000). Identifying Fixations and Saccades in Eye-Tracking Protocols. *Proceedings of the Eye Tracking Research and Applications Symposium*, 71–78. http://doi.org/10.1145/355017.355028

Sammarco, A. (2001). Perceived social support, uncertainty, and quality of life of younger breast cancer survivors. *Cancer Nursing*, *24*(3), 212–219. http://doi.org/10.1097/00002820-200106000-00010

Schmukle, S. C. (2005). Unreliability of the dot probe task. *European Journal of Personality*, *19*(7), 595–605. http://doi.org/10.1002/per.554

Schoorl, M., Putman, P., Van Der Werff, S., & Van Der Does, a. J. W. (2014). Attentional bias and attentional control in Posttraumatic Stress Disorder. *Journal of Anxiety Disorders*, *28*(2), 203–210. http://doi.org/10.1016/j.janxdis.2013.10.001

Schoth, D. E., & Liossi, C. (2016). Biased Interpretation of Ambiguous Information in Patients With Chronic Pain: A Systematic Review and Meta-Analysis of Current Studies. *Health Psychology*, *35*(9), 944–956. http://doi.org/10.1037/hea0000342

Schoth, D. E., Nunes, V. D., & Liossi, C. (2012). Attentional bias towards pain-related information in chronic pain; a meta-analysis of visual-probe investigations. *Clinical Psychology Review*, *32*(1), 13–25. http://doi.org/10.1016/j.cpr.2011.09.004

Sharpe, L., Ianiello, M., Dear, B. F., Nicholson Perry, K., Refshauge, K., & Nicholas, M. K. (2012). Is there a potential role for attention bias modification in pain patients? Results of 2 randomised, controlled trials. *Pain*, *153*(3), 722–731. http://doi.org/10.1016/j.pain.2011.12.014

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*, *19*(9), 1248–1257. http://doi.org/10.1002/ejp.648

Shechner, T., Rimon-Chakir, A., Britton, J. C., Lotan, D., Apter, A., Bliese, P. D., … Bar-Haim, Y. (2014). Attention bias modification treatment augmenting effects on cognitive behavioral therapy in children with anxiety: Randomized controlled trial. *Journal of the American Academy of Child and Adolescent Psychiatry*, *53*(1), 61–71. http://doi.org/10.1016/j.jaac.2013.09.016

Siddall, P. J., & Cousins, M. J. (2004). Persistent pain as a disease entity: implications for clinical management. *Anesthesia and Analgesia*, *99*(2), 510–520, table of contents. http://doi.org/10.1213/01.ANE.0000133383.17666.3A

Simmons, J. P., Nelson, L. D., & Simonsohn, U. (2011). False-Positive Psychology: Undisclosed Flexibility in Data Collection and Analysis Allows Presenting Anything as Significant. *Psychological Science*, *22*(11), 1359–1366. http://doi.org/10.1177/0956797611417632

Simon, D., Craig, K. D., Gosselin, F., Belin, P., & Rainville, P. (2008). Recognition and discrimination of prototypical dynamic expressions of pain and emotions. *Pain*, *135*(1-2), 55–64. http://doi.org/10.1016/j.pain.2007.05.008

Simons, L. E., & Kaczynski, K. J. (2012). The fear avoidance model of chronic pain: Examination for pediatric application. *Journal of Pain*, *13*(9), 827–835. http://doi.org/10.1016/j.jpain.2012.05.002

Sleed, M., Eccleston, C., Beecham, J., Knapp, M., & Jordan, A. (2005). The economic impact of chronic pain in adolescence: Methodological considerations and a preliminary costs-of-illness study. *Pain*, *119*(1-3), 183–190. http://doi.org/10.1016/j.pain.2005.09.028

Smedbråten, B. K., Natvig, B., Rutle, O., & Bruusgaard, D. (1998). Self-reported bodily pain in schoolchildren. *Scandinavian Journal of Rheumatology*, *27*(4), 273–276.

Snelling, J. (1994). The effect of chronic pain on the family unit. *Journal of Advanced Nursing*, *19*(3), 543–551. http://doi.org/10.1111/j.1365-2648.1994.tb01119.x

Spear, L. P. (2000a). The adolescent brain and age-related behavioral manifestations. *Neuroscience and Biobehavioral Reviews*, *24*(4), 417–463. http://doi.org/10.1016/S0149-7634(00)00014-2

Spear, L. P. (2000b). The adolescent brain and age-related behavioral manifestations. *Neuroscience and Biobehavioral Reviews*. http://doi.org/10.1016/S0149-7634(00)00014-2

Spielberger, C. D., Edwards, C. D., Lushene, R. E., Montuori, J., & Platzek, D. (1973). *The State-Trait Anxiety Inventory for Children (preliminary manual)*. Palo Alto, CA: Consulting Psychologists Press.

Stopa, L., & Clark, D. M. (2000). Social phobia and interpretation of social events. *Behaviour Research and Therapy*, *38*(3), 273–283. http://doi.org/10.1016/S0005-7967(99)00043-1

Storch, E. A., Masia-Warner, C., Dent, H. C., Roberti, J. W., & Fisher, P. H. (2004). Psychometric evaluation of the Social Anxiety Scale for Adolescents and the Social Phobia and Anxiety Inventory for Children: Construct validity and normative data. *Journal of Anxiety Disorders*, *18*(5), 665–679. http://doi.org/10.1016/j.janxdis.2003.09.002

Strunin, L., & Boden, L. I. (2004). Family consequences of chronic back pain. *Social Science and Medicine*, *58*(7), 1385–1393. http://doi.org/10.1016/S0277-9536(03)00333-2

Sullivan, M. J. L., Bishop, S. R., & Pivik, J. (1995). The Pain Catastrophizing Scale: Development and validation. *Psychological Assessment*, *7*(4), 524–532. http://doi.org/10.1037/1040-3590.7.4.524

Sullivan, M. J. L., Thorn, B., Haythornthwaite, J. a, Keefe, F., Martin, M., Bradley, L. a, & Lefebvre, J. C. (2001). Theoretical perspectives on the relation between catastrophizing and pain. *The Clinical Journal of Pain*, *17*(1), 52–64. http://doi.org/10.1097/00002508-200103000-00008

Susa, G., Pitică, I., Benga, O., & Miclea, M. (2012). The self regulatory effect of attentional control in modulating the relationship between attentional biases toward threat and anxiety symptoms in children. *Cognition & Emotion*, *26*(6), 1069–1083. http://doi.org/10.1080/02699931.2011.638910

Taghavi, M. R., Moradi, A. R., Neshat-Doost, H. T., Yule, W., & Dalgleish, T. (2000). Interpretation of ambiguous emotional information in clinically anxious children and adolescents. *Cognition & Emotion*, *14*(6), 809–822. http://doi.org/10.1080/02699930050156645

Thorn, B. E. (2004). Cognitive therapy for chronic pain: A step-by-step guide. *(2004).Cognitive Therapy for Chronic Pain: A Step-by-Step Guide.xxiv, 278 pp.New York, NY, US: Guilford Press; US*. Retrieved from http://ovidsp.ovid.com/ovidweb.cgi?T=JS&CSC=Y&NEWS=N&PAGE=fulltext&D=psyc4&AN=2005-02532-000\nhttp://nhs5195535.resolver.library.nhs.uk/?sid=OVID:psycdb&id=pmid:&id=doi:&issn=&isbn=1572309792&volume=&issue=&spage=&pages=&date=2004&title=Cognitive+therapy+

Till, B. D., & Priluck, R. L. (2000). Stimulus generalization in classical conditioning: An initial investigation and extension. *Psychology & Marketing*, *17*(1), 55–72.

Todd, J., Sharpe, L., & Colagiuri, B. (2016). Attentional bias modification and pain: The role of sensory and affective stimuli. *Behaviour Research and Therapy*, *83*, 53–61. http://doi.org/10.1016/j.brat.2016.06.002

Todd, J., Sharpe, L., Johnson, A., Nicholson, K., Colagiuri, B., & Dear, B. F. (2015). Towards a new model of attentional biases in the development, maintenance, and management of pain. *Pain*, *156*(9), 1589–1600. http://doi.org/10.1097/j.pain.0000000000000214

Tran, S. T., Jastrowski Mano, K. E., Hainsworth, K. R., Medrano, G. R., Khan, K. A., Weisman, S. J., & Davies, W. H. (2015). Distinct influences of anxiety and pain catastrophizing on functional outcomes in children and adolescents with chronic pain. *Journal of Pediatric Psychology*, *40*(8), 744–755. http://doi.org/10.1093/jpepsy/jsv029

Tsang, A., Von Korff, M., Lee, S., Alonso, J., Karam, E., Angermeyer, M. C., … Watanabe, M. (2008). Common Chronic Pain Conditions in Developed and Developing Countries: Gender and Age Differences and Comorbidity With Depression-Anxiety Disorders. *Journal of Pain*, *9*(10), 883–891. http://doi.org/10.1016/j.jpain.2008.05.005

Turk, D. C. (2002). A diathesis-stress model of chronic pain and disability following

traumatic injury. *Pain Research & Management: The Journal of the Canadian Pain Society*, *7*(1), 9–19.

Van Damme, S., Crombez, G., & Eccleston, C. (2004). Disengagement from pain: the role of catastrophic thinking about pain. *Pain*, *107*(1–2), 70–76. http://doi.org/http://dx.doi.org/10.1016/j.pain.2003.09.023

Van Damme, S., Legrain, V., Vogt, J., & Crombez, G. (2010). Keeping pain in mind: A motivational account of attention to pain. *Neuroscience and Biobehavioral Reviews*, *34*(2), 204–213. http://doi.org/10.1016/j.neubiorev.2009.01.005

van der Veek, S. M. C., Derkx, B. H. F., Plak, R. D., Benninga, M. a, Boer, F., Lindauer, R. J. L., & de Haan, E. (2014). Attentional Bias to Activity of Different Parts of the Body in Children With Functional Abdominal Pain: An Experimental Study. *Journal of Pediatric Psychology*, *39*(2006), 1–12. http://doi.org/10.1093/jpepsy/jsu004

Van Ryckeghem, D. M. L., Crombez, G., Goubert, L., De Houwer, J., Onraedt, T., & Van Damme, S. (2013). The predictive value of attentional bias towards pain-related information in chronic pain patients: A diary study. *Pain*, *154*(3), 468–475. http://doi.org/10.1016/j.pain.2012.12.008

Van Ryckeghem, D. M. L., Crombez, G., Van Hulle, L., & Van Damme, S. (2012). Attentional bias towards pain-related information diminishes the efficacy of distraction. *Pain*, *153*(12), 2345–2351. http://doi.org/10.1016/j.pain.2012.07.032

Vancleef, L. M. G., Hanssen, M. M., & Peters, M. L. (2016). Are individual levels of pain anxiety related to negative interpretation bias? An examination using an ambiguous word priming task. *European Journal of Pain*, *20*(5), 833–841. http://doi.org/10.1002/ejp.809

Vancleef, L. M. G., & Peters, M. L. (2006). Pain catastrophizing, but not injury/illness sensitivity or anxiety sensitivity, enhances attentional interference by pain. *Journal of Pain*, *7*(1), 23–30. http://doi.org/10.1016/j.jpain.2005.04.003

Vancleef, L. M. G., & Peters, M. L. (2008). Examining content specificity of negative interpretation biases with the Body Sensations Interpretation Questionnaire (BSIQ). *Journal of Anxiety Disorders*, *22*(3), 401–415. http://doi.org/10.1016/j.janxdis.2007.05.006

Vancleef, L. M. G., Peters, M. L., & De Jong, P. J. (2009). Interpreting ambiguous health and bodily threat: Are individual differences in pain-related vulnerability constructs associated with an on-line negative interpretation bias? *Journal of Behavior Therapy and Experimental Psychiatry*, *40*(1), 59–69. http://doi.org/10.1016/j.jbtep.2008.03.004

Verhoeven, K., Crombez, G., Eccleston, C., Van Ryckeghem, D. M. L., Morley, S., & Van Damme, S. (2010). The role of motivation in distracting attention away from pain: An experimental study. *Pain*, *149*(2), 229–234. http://doi.org/http://dx.doi.org/10.1016/j.pain.2010.01.019

Vervoort, T., Caes, L., Crombez, G., Koster, E. H. W., Van Damme, S., Dewitte, M., & Goubert, L. (2011). Parental catastrophizing about children's pain and selective attention to varying levels of facial expression of pain in children: A dot-probe study. *Pain*, *152*(8), 1751–1757. http://doi.org/10.1016/j.pain.2011.03.015

Vervoort, T., Caes, L., Trost, Z., Notebaert, L., & Goubert, L. (2012). Parental attention to their child's pain is modulated by threat-value of pain. *Health Psychology*, *31*(5), 623–631. http://doi.org/10.1037/a0029292

Vervoort, T., Craig, K. D., Goubert, L., Dehoorne, J., Joos, R., Matthys, D., … Crombez, G. (2008). Expressive dimensions of pain catastrophizing: A comparative analysis of school children and children with clinical pain. *Pain*, *134*(1-2), 59–68. http://doi.org/10.1016/j.pain.2007.03.038

Vervoort, T., Eccleston, C., Goubert, L., Buysse, A., & Crombez, G. (2010). Children's

catastrophic thinking about their pain predicts pain and disability 6 months later. *European Journal of Pain*, *14*(1), 90–96. http://doi.org/10.1016/j.ejpain.2009.03.001

Vervoort, T., Goubert, L., & Crombez, G. (2009). The relationship between high catastrophizing children's facial display of pain and parental judgment of their child's pain. *Pain*, *142*(1-2), 142–148. http://doi.org/10.1016/j.pain.2008.12.028

Vervoort, T., Goubert, L., Eccleston, C., Bijttebier, P., & Crombez, G. (2006). Catastrophic thinking about pain is independently associated with pain severity, disability, and somatic complaints in school children and children with chronic pain. *Journal of Pediatric Psychology*, *31*(7), 674–683. http://doi.org/10.1093/jpepsy/jsj059

Vervoort, T., & Trost, Z. (2015). The interpersonal function of pain. *Pain*, *157*(4), 1. http://doi.org/10.1097/j.pain.0000000000000438

Vervoort, T., Trost, Z., Prkachin, K. M., & Mueller, S. C. (2013). Attentional processing of other's facial display of pain: An eye tracking study. *Pain*, *154*(6), 836–844. http://doi.org/10.1016/j.pain.2013.02.017

Vervoort, T., Trost, Z., Sütterlin, S., Caes, L., & Moors, A. (2014). Emotion regulatory function of parent attention to child pain and associated implications for parental pain control behaviour. *Pain*, *155*(8), 1453–1463. http://doi.org/10.1016/j.pain.2014.04.015

Vervoort, T., Trost, Z., & Van Ryckeghem, D. M. L. (2013). Children's selective attention to pain and avoidance behaviour: The role of child and parental catastrophizing about pain. *Pain*, *154*(10), 1979–1988. http://doi.org/10.1016/j.pain.2013.05.052

Vlaeyen, J. W. S., & Linton, S. J. (2000). Fear-avoidance and its consequences in chronic musculoskeletal pain: A state of the art. *Pain*, *85*(3), 317–332. http://doi.org/10.1016/S0304-3959(99)00242-0

Vlaeyen, J. W. S., & Linton, S. J. (2012). Fear-avoidance model of chronic musculoskeletal pain: 12 years on. *Pain*, *153*(6), 1144–1147. http://doi.org/10.1016/j.pain.2011.12.009

Von Baeyer, C. L., Piira, T., Chambers, C. T., Trapanotto, M., & Zeltzer, L. K. (2005). Guidelines for the cold pressor task as an experimental pain stimulus for use with children. *Journal of Pain*, *6*(4), 218–227. http://doi.org/10.1016/j.jpain.2005.01.349

Walker, L. S., & Greene, J. W. (1991). The functional disability inventory: measuring a neglected dimension of child health status. *Journal of Pediatric Psychology*, *16*(1), 39–58. http://doi.org/10.1093/jpepsy/16.1.39

Wang, D. Y. D., Richard, F. D., & Schmular, J. (2014). Training with Action-Video Games and Attentional Resources: Effect of Video Game Playing on a Flanker Task. *International Conference on Humanity and Social Science (Ichss 2014)*, 170–174.

Wardley, A., Davidson, N., Barrett-Lee, P., Hong, A., Mansi, J., Dodwell, D., … Cameron, D. (2005). Zoledronic acid significantly improves pain scores and quality of life in breast cancer patients with bone metastases: a randomised, crossover study of community vs hospital bisphosphonate administration. *British Journal of Cancer*, *92*(10), 1869–1876. http://doi.org/10.1038/sj.bjc.6602551

Wilson, E., & MacLeod, C. (2003). Contrasting two accounts of anxiety-linked attentional bias: Selective attention to varying levels of stimulus threat intensity. *Journal of Abnormal Psychology*, *112*(2), 212–218. http://doi.org/10.1037/0021-843X.112.2.212

Wonghongkul, T., Dechaprom, N., Phumivichuvate, L., & Losawatkul, S. (2006). Uncertainty Appraisal Coping and Quality of Life in Breast Cancer Survivors. *Cancer Nursing*, *29*(3), 250–257. http://doi.org/10.1097/00002820-200605000-00014

Zale, E. L., Lange, K. L., Fields, S. A., & Ditre, J. W. (2013). The relation between pain-related fear and disability: A meta-analysis. *Journal of Pain*, *14*(10), 1019–1030. http://doi.org/10.1016/j.jpain.2013.05.005

Appendices

9. Appendices

A

Validation of ABM Stimulus Sets 1 and 2 for Chapter Four

At the post-training assessment session participants were asked to rate each child pain face for pain intensity using a 0-10 NRS (i.e., 'How much pain has the child displayed on the picture; anchors; 'no pain at all'; 'a lot of pain'). Pictures were presented on a computer screen using Office PowerPoint in a randomized order that was fixed across participants. Picture ratings were averaged for each stimulus type (pain, neutral), resulting in two mean pain intensity ratings ranging from 0-10. This allowed examining whether participants' perception of the child facial expressions (pain, neutral) matched the experimenter-selected categories.

A paired samples *t*-test revealed a significant difference between ratings of the child pain and neutral face stimuli. As expected, pain facial expressions (M = 6.45, SD = 1.39) were rated significantly higher (i.e., expressing significantly more pain) than neutral facial expressions (M = 1.17, SD = 0.93; t (64) = 28.99, p < .001), thus confirming stimulus categories.

9. Appendices

B

List of Pain and Neutral words Used in ABM for Chapter Four

Pain	Neutral
ache	clam
agony	packs
beating	farming
bellyache	nightwear
biting	posted
broken	joined
burning	washing
choking	tracing
cold	main
crack	crown
cramp	flank
crushing	advising
cutting	writing
drilling	evenings
flickering	rediscover
gassy	wispy
gnawing	notepad
grinding	doubling
gritty	canopy
hard	such
headache	reserves
hurt	draw
itch	huts
jabbing	coining
lock	rice
migraine	steamers
numb	rosy
ouch	grid
pain	bird

piercing	adapting
pinch	bikes
pounding	pitching
pressing	switched
pricking	stemming
pulling	sending
rub	log
scraping	gleaming
sharp	basic
shooting	customer
sick	calm
snap	goats
sore	neat
squeezing	directing
stabbing	stocking
stiff	swiss
sting	toast
tummyache	backlight
swollen	nesting
tearing	shaping
tender	barrel
throbbing	resorting
twinging	described
tingling	stacking
tugging	winging

C

Per-Protocol Analyses for Chapter Four

Attention Bias Analyses

Attention Bias at Baseline

There were no significant differences between reaction times to congruent or incongruent trials at baseline, (t (62) = 0.06, p = .95), and the calculated bias score was not significantly different from zero at baseline (t (62) = -0.06, p = .95), indicating no attentional biases to pain-related stimuli.

Change in Attention Bias following Training

A 2 (Congruency: congruent, incongruent) x 2 (Time: baseline, post-treatment) x 3 (Group: ABM, Placebo, Waitlist) ANOVA was conducted for dot-probe scores to assess whether a reliable training effect of ABM could be determined. Analyses revealed a main effect for time (F (1, 60) = 97.19, p < .001, η_p^2 = .62), indicating that all participants, regardless of training, had faster RTs at the post-training assessment compared to the baseline assessment. There were no main effects of congruency (F (1, 60) = 1.85, p = .18, η_p^2 = .03), or group (F (2, 60) = 1.27, p = .29, η_p^2 = .04), nor two-way interactions for time x group (F (2, 60) = 2.62, p = .08, η_p^2 = .08), congruency x group (F (2, 60) = .001. p =.10, η_p^2 = .00),

or time x congruency (F (1, 60) = 1.60, p = .21, η_p^2 = .03). There was also no three-way interaction for time x congruency x group (F (2, 60) = 0.42, p = .66, η_p^2 = .01). Thus, results indicated that the predicted training effect was not observed.

Primary Outcome Measures

A series of 2 (Time: baseline, post-treatment) x 3 (Condition: ABM, Placebo, Waitlist) ANOVAs were conducted on pain symptoms, i.e., the primary outcome measures (pain intensity at most problematic body site, average pain intensity, and pain duration in the last week). There was a marginally significant main effect of time for pain duration (F (1, 61) = 3.96, p = .05, η_p^2 = .06), indicating that all participants, regardless of training, experienced pain for less time each day. However, contrary to our hypotheses, there were no interaction effects.

Secondary Outcome Measures

A series of 2 (Time: baseline, post-training) x 3 (Condition: ABM, Placebo, Waitlist) ANOVAs were conducted on secondary outcome measures. There were main effects of time for functional disability (F (1, 61) = 17.42, p < .001, η_p^2 = .22), pain catastrophizing (F (1, 61) = 18.22, p < .001, η_p^2 = .23), generalised anxiety (F (1, 61) = 6.47, p = .01, η_p^2 = .10), sit-to-stand task (F (1, 61) = 6.17, p = .02, η_p^2 = .09), and cardio wall task (F (1, 61) = 18.91, p < .001, η_p^2 = .24), indicating that participants improved over time on these measures, regardless of training group. The only significant interaction effect was for generalised anxiety (F (2, 61) = 5.15, p = .01, η_p^2 = .14). Bonferroni-corrected analyses of simple main effects revealed that there was a significant decrease in generalised anxiety from baseline to post-training

assessment in the ABM group (p = .002) and the placebo group (p = .03), but not the waitlist group (p = .27) No other interaction effects reached significance.

Attention Control Analyses

Change in Attention Control after Training

To examine whether ABM training changed self-reported attention control, we conducted a 2 (Time: baseline, post-training) x 3 (Condition: ABM, Placebo, Waitlist) ANOVA with the Attention Control Scale (ACS) score as the outcome variable. There was a main effect of time (F (1, 61) = 4.17, p = .05, η_p^2 = .06), indicating that participants reported improved attention control at the post-training assessment compared to baseline. There was no interaction effect, indicating that ABM training did not lead to changes in self-reported attention control compared with placebo training or no training (waitlist).

To examine whether ABM training changed experimentally-measured attention control, we conducted a 2 (Congruency: congruent, incongruent) x 2 (Time: baseline, post-treatment) x 3 (Group: ABM, placebo, waitlist) ANOVA for RTs on the flanker task. There was a main effect of congruency (F (1, 61) = 146.03, p < .001, η_p^2 = .71), indicating that participants were slower on incongruent than congruent trials. There were no other main effects, and no interactions effects.

Moderation of Training Effect by Attention Control

To examine whether baseline levels of self-reported attention control moderated training efficacy, we performed the same series of ANOVAs described above for primary outcome measures and dot-probe indices, but including the centred ACS score as a covariate. Analyses revealed a significant time x group x attention control interaction for most problematic pain intensity (F (2, 57) = 3.47, p = .04, η_p^2 = .11). To interpret this three-way

interaction, we first performed three additional ANOVAs as described above, but separately for each group (ABM, placebo, waitlist). These additional analyses revealed a significant time x attention control interaction for the waitlist group (F (1, 18) = 8.88, p = .01, η_p^2 = .33), but not for the ABM (F (1, 20) = 0.49, p = .49, η_p^2 = .02) or placebo group (F (1, 19) = 0.06, p = .81, η_p^2 = .003). Thus, attention control was a significant moderator for the waitlist but not the ABM or placebo groups. To aid interpretation of the significant two-way interaction for the waitlist group, we computed a pain change score by subtracting participants' most problematic pain at post-training assessment from their most problematic pain at baseline. A bivariate correlation revealed that participants (in the waitlist group) with higher self-reported attention control at baseline reported significantly reduced pain at the post-training assessment (r = -.58, p = .01). There were no other significant three-way interactions for primary outcome measures, or for dot-probe indices, and the main effects of time for pain duration and dot-probe indices remained unchanged (data that remained unchanged are not reported again).

To examine whether baseline levels of experimentally-measured attention control moderated training efficacy, we again performed the same series of ANOVAs described above for primary outcome measures and dot-probe indices, but this time including a centred interference score as a covariate. This interference score was derived from the flanker task by subtracting mean RTs on congruent from incongruent trials. Thus a higher interference score indicates lower attention control. Unlike in the ITT analyses, the main effect of time for pain duration was no longer significant when controlling for experimentally-measured attention control (F (1, 58) = 1.41, p = .24, η_p^2 = .02). This is the only finding that differs between ITT and PP analyses. There were no significant two- or three-way interaction effects for primary

outcome measures or for dot-probe indices, and the main effect of time for dot-probe indices remained unchanged (data that remained unchanged are not reported again).

9. Appendices

D

AIBT Task Items for Chapters Five and Six

Ambiguous Social Situation	Benign Word	Negative Word
Your school is looking for a new person to join their debating team. You ask for more details. After hearing these, you decide you would be	welcomed	rejected
You really like the new kid at school. At a birthday party the two of you talk for a long time. When you meet the next day at school, they smile at you and then leave the room quickly when you come in. You are sure that this is because they find you quite	attractive	irritating
Your maths teacher likes to give short quizzes at the beginning of each lesson. One day you and one of the cool kids are picked to do the quiz. The other kid does not take the quiz seriously and gets all his answers wrong whereas you do quite well. You are sure that your classmates think you are	smart	geeky
You receive a notification that one of your classmates has put a comment on your picture on Facebook. While opening the webpage you think that it will be something	nice	nasty
You raise your hand to give your views during a debate in the English lesson. When the teacher picks you, you think that the others will find your opinions	important	ridiculous
During a year group assembly your drama teacher asks you to make a quick announcement about the upcoming play. You try to make it interesting and some people begin to giggle. This is because your jokes are	funny	stupid
You are asked to be the DJ at the school's disco night. While playing music you see a few of your classmates. You can see that they think your choice of music is	awesome	silly
Your best friend invites you to go out with their new friends from the drama club. You hesitate at first but then agree to come along. At the end of the evening you think that the other people thought that you were	lovely	dull

Ambiguous Bodily Threat Situation	Benign Word	Negative Word
Your dad jumps out of his chair and puts his hands to his face, making a loud noise. He is	surprised	hurt
You see a boy breathing heavily. His chest is quickly going up and down. He is	exercising	asthmatic
Your friend tells you that he visited his doctor this morning. He has received test results. The results say that he is	fine	unwell
Yesterday your bicycle was hit by a car. You will not be able to cycle for a while because the car broke your	bike	leg
Your friend takes a pill every morning at breakfast. He takes this every day. The pill is a	vitamin	medicine
It is 10am on a Monday and you are still in bed. You are at home because you have a	holiday	cold
You finally got your test results. You have been worried about them all week. The results are from your	school	doctor
Someone kicks a ball and it hits you in the face. In the mirror you see your face is covered in	mud	blood

E

Validity of Social AIBT Items for Chapter Five

Using the final AIBT task, we aimed to explore the validity of the social items by investigating whether interpretations of these items significantly correlated with social anxiety scores. Indeed, previous studies have reported strong associations between self-reported social anxiety and negative interpretations of ambiguous social situations (Amir, Foa, & Coles, 1998; Butler & Mathews, 1983; Franklin, Huppert, Langner, Leiberg, & Foa, 2005; Miers, Blöte, Bögels, & Westenberg, 2008; Stopa & Clark, 2000; Wilson & Rapee, 2005). We aimed to replicate these findings using the AIBT task's social items, to support the validity of our new task. Thus, we included a measure of social anxiety in the final sample (see below), and we conducted bivariate correlations between social anxiety and ratings of social situations. These analyses yielded significant positive associations between social anxiety and negative interpretations of social situations (r = .61, p < .001) and belief in those interpretations (r = .44, p < .001), as well as significant negative associations with benign interpretations of social situations (r = -.42, p < .001) and belief in those interpretations (r = -.40, p < .001).

Amir, N., Foa, E. B., & Coles, M. E. (1998). Negative interpretation bias in social phobia. Behaviour Research and Therapy, 36(10), 945–957. http://doi.org/10.1016/S0005-7967(98)00060-6

Butler, G., & Mathews, A. (1983). Cognitive processes in anxiety. Advances in Behaviour Research and Therapy, 5(1), 51–62. http://doi.org/10.1016/0146-6402(83)90015-2

Franklin, M. E., Huppert, J., Langner, R., Leiberg, S., & Foa, E. B. (2005). Interpretation bias: A comparison of treated social phobics, untreated social phobics, and controls. Cognitive Therapy and Research, 29(3), 289–300. http://doi.org/10.1007/s10608-005-2412-8

Miers, A. C., Blöte, A. W., Bögels, S. M., & Westenberg, P. M. (2008). Interpretation bias and social anxiety in adolescents. Journal of Anxiety Disorders, 22(8), 1462–1471. http://doi.org/10.1016/j.janxdis.2008.02.010

Stopa, L., & Clark, D. M. (2000). Social phobia and interpretation of social events. Behaviour Research and Therapy, 38(3), 273–283. http://doi.org/10.1016/S0005-7967(99)00043-1

Wilson, J. K., & Rapee, R. M. (2005). Interpretative biases in social phobia: Content specificity and the effects of depression. Cognitive Therapy and Research, 29(3), 315–331. http://doi.org/10.1007/s10608-005-2833-6

F

Forced Choice Data for Chapter Five

Pain catastrophizing and interpretation bias

To examine the association between pain catastrophizing and interpretations, a 2 (block) x 2 (context) ANCOVA was conducted with pain catastrophizing score entered as a covariate (Table A1 presents the *M*s and *SD*s of this analysis. Means closer to 1 reflect more negative word choices. Means closer to 0 reflect more benign word choices). The multivariate test yielded significant effects for **pain catastrophizing**, $F(1, 113) = 11.07$, $p = .001$, partial $\eta^2 = .09$, and **block**, $F(1, 113) = 7.60$, $p < .01$, partial $\eta^2 = .06$. There was also a significant two-way interaction for **context x block**, $F(1, 113) = 5.55$, $p < .05$, partial $\eta^2 = .05$. Pain catastrophizing did not interact with context or block to form any two- or three-way interactions.

The main effect of block occurred because, across context, participants gave stronger ratings for how easily interpretations came to mind (M = 0.49, SD = .19) than their belief in interpretations (M = 0.37, SD = .19). Decomposing the context x block interaction revealed that participants gave significantly stronger ratings when considering whether interpretations came to mind compared with their belief in those interpretations for both the bodily threat items ($t(114) = -7.42$, $p < .001$) and social items ($t(114) = -4.10$, $p < .001$). However effect was larger for the bodily threat items (interpretation generation; M = 0.51, SD = 0.25;

interpretation belief: M = 0.35, SD = .21) than the social items (interpretation generation; M = 0.46, SD = 0.26; interpretation belief: M = 0.38, SD = .25).

To further examine the main effect of **pain catastrophizing**, we conducted a Pearson correlation between pain catastrophizing and participants' word choice, collapsed across block and context. This analysis revealed that adolescents with higher levels of pain catastrophizing were significantly more likely to select negative interpretations than adolescents with low levels of pain catastrophizing (r = .30, p = .001).

Table A1. *Means and SDs (in brackets) for the AIBT ratings data*

Interpretation generation (Block 1)	
Bodily threat word choice	0.51 (0.20)
Social word choice	0.46 (0.26)
Interpretation belief (Block 2)	
Bodily threat word choice	0.35 (0.21)
Social word choice	0.38 (0.25)

Pain experiences and interpretation bias

To examine the association between recent pain experiences and interpretations, a 2 (block) x 2 (context) ANCOVA was conducted with pain experiences score entered as a covariate. The multivariate test yielded significant effects for **recent pain experiences**, $F(1, 113) = 12.18$, p =.001, partial $\eta^2 = .10$, and **block**, $F(1, 113) = 10.46$, p <.01, partial $\eta^2 = .09$. There was also a significant two-way interaction for **context x block**, $F(1, 113) = 4.77$, p <.05, partial $\eta^2 = .04$. Pain catastrophizing did not interact with context or block to form any two- or three-way interactions. As the main effects and interaction effects not including pain experiences were explored earlier, these were not explored again here.

To further examine the main effect of **recent pain experiences**, we conducted a Pearson correlation between recent pain experiences and participants' word choice, collapsed across block and context. This analysis revealed that adolescents who experienced more pain

were significantly more likely to select negative interpretations than adolescents with low levels of pain catastrophizing (r = .31, p = .001).

Testing for mediator effects

Similarly to the ratings data, the analysis using the forced choice data reported above confirmed that a negative interpretation bias was associated with both higher pain catastrophizing and higher experiences of recent pain. Analysis was therefore performed to determine whether a negative interpretation bias mediated the association between pain catastrophizing and recent pain experiences. Following analyses for the ratings data, given that context (bodily threat/social) and block (interpretation generation/belief) did not interact with valence and pain catastrophizing or recent pain, we first performed the mediation analysis using the mean word choice score that was collapsed across context and block. However, given that we may expect a more specific role of bodily threat interpretations to act as a mediator between two pain-related variables, we also performed the mediation analysis separately for the bodily threat items and the social items.

First, when using the word choice score collapsed across context and block, there was a significant indirect effect of pain catastrophizing on recently experienced pain through interpretation bias, b = 0.04, BCa CI [0.008, 0.112]. This represents a small-to-medium effect, kappa^2 = .064, 95% BCa CI [0.015, 0.161]. Next, when using the word choice score for bodily threat items only (collapsed across block), there was again a significant indirect effect of pain catastrophizing on recently experienced pain through interpretation bias, b = 0.03, BCa CI [0.003, 0.096]. This represents a small-to-medium effect, kappa^2 = .053, 95% BCa CI [0.068, 0.147]. Finally, when using the word choice score for social items only (collapsed across block), there was not a significant indirect effect, b = 0.02, BCa CI [-0.010, 0.081]. As with the ratings data, the analyses with the forced choice data indicates that, when

considered separately, only negative interpretations of ambiguous information regarding pain and bodily threat mediated the association between pain catastrophizing and recent pain experiences. A negative social interpretation bias did not play a mediating role.

G

Extra Data Tables for Chapter Six

Table A2. *All main & interaction effects from repeated-measures ANOVA*

	F	**Sig**	**Partial Eta Square**
GROUP	0.10	.750	.001
context	118.11	.000	.461
context * GROUP	5.43	.021	.038
block	42.56	.000	.236
block * GROUP	1.27	.261	.009
valence	10.32	.002	.070
valence * GROUP	4.53	.035	.032
context * block	8.93	.003	.061
context * block * GROUP	0.06	.805	.000
context * valence	0.002	.962	.000
context * valence * GROUP	0.08	.784	.001
block * valence	80.14	.000	.367
block * valence * GROUP	0.50	.482	.004
context * block * valence	10.60	.001	.071
context * block * valence GROUP	6.39	.013	.044

Table A3. *All main & interaction effects from repeated-measures ANOVAs performed separately for bodily threat and social items*

	F	**Sig**	**Partial Eta Squared**
Bodily Threat Items			
block	43.511	.000	.240
block * GROUP	1.033	.311	.007
valence	10.977	.001	.074
valence * GROUP	3.892	.051	.027
block * valence	91.525	.000	.399
block * valence * GROUP	4.914	.028	.034
GROUP	1.680	.197	.012
Social Items			
block	20.848	.000	.131
block * GROUP	0.879	.350	.006
valence	4.919	.028	.034
valence * GROUP	2.630	.107	.019
block * valence	23.590	.000	.146
block * valence * GROUP	0.886	.348	.006
GROUP	0.605	.438	.004

Table A4: *Pearson correlation coefficients for AIBT task social items and measures of anxious/depressive symptomatology*

	1	2	3	4	5	6
1. Generalized anxiety	---	.63***	.45***	-.30***	.23**	-.16
2. Depression		---	.34***	-.33***	.29**	-.29**
3. Social_Generation_Negative			---	-.44***	.51***	-.22*
4. Social_Generation_Benign				---	-.33***	.59***
5. Social_Belief_Negative					---	-.43***
6. Social_Belief_Benign						---

*p < .05; **p < .01; ***p < .001