UNIVERSITY OF DERBY

EXPLORING COGNITIVE BIASES IN PAIN: INVESTIGATING ATTENTION, INTERPRETATION AND MEMORY BIAS.

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Doctor of Philosophy 2023

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List of Abbreviations

AB – *Attentional Bias.*

AIBT – *Adolescent Interpretation Bias Task.*

AR – *Adaptive Response.*

CFS – *Chronic Fatigue Syndrome.*

CH – *Chronic Headache.*

CLBP – *Chronic Low Back Pain.*

DASS-21 – *Depression, Anxiety and Stress Scale (21-item).*

DASS-42 – *Depression, Anxiety and Stress Scale (42-item).*

ER – *Endurance Response.*

FAMP – *Fear-avoidance Model of Pain.*

FAR – *Fear Avoidance Response.*

GAPED – *Geneva Affective Picture Database.*

GCT – *Gate Control Theory.*

IAPS – *International Affective Picture System.*

IASP – *International Association for the Study of Pain.*

IB – *Interpretation Bias.*

IBS – *Irritable Bowel Syndrome.*

IFCF – *Integrated Functional Contextual Framework.*

MB – *Memory Bias.*

MPSM – *Misdirected Problem-Solving Model.*

NPC – *Non-Pain Control.*

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PICS – *Psychological Image Collection at Stirling.*

R/K – *Remember/Know.*

RPEQ – *Recent Pain Experiences Questionnaire.*

SEMP – *Schema Enmeshment Model of Pain.*

TIM – *Threat Interpretation Model.*

UK – *United Kingdom.*

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Preface

I declare that this thesis was composed by myself, that the work contained herein is my own except where explicitly stated otherwise in the text, and that this work has not been submitted for any other degree or professional qualification except as specified. Part of this work, specifically content from Chapter 4 (measuring interpretation bias using ambiguous scenarios), has now been published in *Frontiers in Psychology*, but this work formed part of the original programme of research, with the published work a later version.

Citation:

Gaffiero, D., Staples, P., Staples, V., & Maratos, F. A. (2021). Interpretation Biases in Pain: Validation of Two New Stimulus Sets. *Frontiers in Psychology*, *12*. https://doi.org/10.3389/fpsyg.2021.784887

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Abstract

Cognitive-affective models posit that cognitive biases contribute to the aetiology and maintenance of chronic pain. In chronic pain, it is argued that cognitive biases encapsulate interpretation bias, attentional bias, and memory bias. These biases are suggested to exert their influence through the preferential processing of information pertaining to pain, bodily-threat, and harm. Research exploring multiple cognitive biases within the context of a single study is limited. Thus, the role, nature and interaction of these cognitive biases remains poorly understood.

This programme of research aimed to address these limitations. Studies 1 and 2 progressed the development and validation of stimulus sets suitable for measuring pain-related attention and interpretation biases in adults. Study 3 then investigated whether a single experience of pain influences cognitive biases in a pain-free sample subjected to acute pain; and study 4 investigated the measurement of cognitive biases, in a chronic pain (vs. non-pain control) sample.

Study 1 resulted in the development of two stimulus sets categorised via varying degrees of pain intensity (neutral, low, high) and threat (low, medium, high) to enable rigorous investigation of attentional bias. Study 2 resulted in the development and validation of two ambiguous scenario stimulus sets to enable rigorous investigation of interpretation (and subsequently memory) bias utilising i) forced-choice and ii) free-response paradigms. Supplementary analyses indicated that recent pain experiences positively correlated with the endorsement of pain/pain-illness interpretations of the ambiguous scenarios. Study 3 revealed that a single acute pain experience was not sufficient to influence cognitive biases. However, individuals subjected to a warm water control (as opposed to a cold-pressor task) showed increased attention towards pain-related information, increased recall of pain words immediately following the warm water control, and greater recognition of non-pain words. Additionally, in the acute pain group, measures of pain threshold and tolerance were associated with attention, interpretation, and memory biases. These results indicate a potentially pleasant experience can bias attention toward pain stimulus processing and the importance of pain sensitivity as an influencing cognitive bias factor. Consistent with Study 3, Study 4 provided no evidence of pain-related interpretation or recall biases. However, the chronic pain group

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exhibited poorer overall recognition performance, compared to their pain-free counterparts. Cross-bias correlations further revealed that as the number of ambiguous scenarios interpreted as pain/pain-illness related increased, so too did the number of pain/pain-illness solutions correctly recalled, irrespective of pain experience. However, correlations between cognitive biases for the non-pain/non-pain illness stimuli were exclusive to the pain-free group. This indicates that the chronic pain group processed scenarios interpreted in a pain/pain-illness manner differently than those they interpreted in a non-pain/non-pain illness manner.

Overarching conclusions indicate that individuals with lower pain thresholds and tolerance are more likely to display biased attention, interpretation, and memory favouring pain/pain-illness information; and that individuals with chronic pain display impaired recognition for pain/pain-illness related information. A detailed discussion of these findings is presented in the final chapter, including the proposition of a Pain Sensitivity Model in understanding the role of cognitive biases in pain.

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Acknowledgements

Whilst my name is located under the title of this thesis, and it is me who will be subsequently credited – I wish to acknowledge the individuals that have inspired me, supported me in times of need, gave useful feedback, and most importantly put me in a position I never thought I would be in – submitting a PhD thesis! Below I would like to express my gratitude to these individuals and acknowledge their contribution.

Firstly, I would like to express my gratitude to a special teacher, ***Tracie Barnes***, who sparked my initial enthusiasm for Psychology. Tracie's sessions were always informative and engaging and delivered with passion. She had an abundance of patience, listened, understood and was empathetic towards me whenever I struggled (which was quite often). Her excellent teaching had a notable impact on my academic performance too, helping me transform from a distinctively average sixth form student into a good one! Aside from a transformation in grades, Tracie also helped me to develop more self-confidence and motivated me to succeed. She was the first teacher to show me that with hard-work and dedication I could achieve something. Without her support and guidance during these years, I truly believe I would not be sat here writing this now. In a profession where students come and go after a couple of years, I hope you realise that your excellent teaching has and will continue to have a profound and long-lasting impact on students. As Freud once said "one day, in retrospect, the years of struggle will strike you as the most beautiful" – so Tracie, thank you, this one is for you!

Next, I would like to thank my Director of Studies, ***Professor Frances A. Maratos***. I first came to know Frankie after being taught by her during my Undergraduate Degree. Her sessions in Biological, Cognitive and Abnormal Psychology sparked my interest in attention, cognition, and emotional disorders. Her knowledge was always passionately delivered in an informative and accessible manner, and I distinctively remember feeling privileged to have attended a university with her as a Lecturer. In the second year of my Undergraduate degree Frankie supported me to write an application for an Undergraduate Research Scholarship Scheme which involved conducting research in the form of a mini-PhD style project. Not only was this application successful and I awarded the scholarship, but during this period Frankie taught me a variety of key skills including the use of psychophysiological methods (i.e., eye-tracking technology). Without these skills I most certainly would not have had the knowledge

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or experience necessary to be able to conduct several studies presented in this PhD thesis. Frankie was one of the first lecturers to teach me how to conduct all aspects of the research process, from greeting participants to task execution. It was this insightful experience at Undergraduate level that led me to approaching her to be my supervisor for my master's Thesis and Director of Studies for my PhD. Aside from Frankie's outstanding teaching skills, she is one of the most inspiring women I have met. Throughout this four-year period, Frankie has encouraged me, supported me through the challenges I have faced, and spent considerable time reviewing my work. I feel privileged to have had Frankie as my Director of Studies and thus will always be indebted to her.

Now, I turn my focus to a man I like to call the 'Godfather of statistics, ***Dr Paul Staples***. Paul is one of the most passionate lecturers at the University of Derby and is one, of very few, that can make statistics enjoyable to learn. His background knowledge of the advanced inferential tests used in Psychology is frightening. But a key skill of Paul's is his ability to transform complex information, into materials that can be grasped and understood with ease. The materials he produces to accompany his sessions are outstanding and have proved useful when analysing data for various chapters of my PhD thesis! I first met Paul during an advanced research methods module during my MSc and immediately became fond of him. Paul's contribution to my understanding of statistics cannot be understated – in previous research methods modules I struggled, but under Paul's teaching I excelled during my MSc and achieved a very high grade. Paul has also been a fantastic supervisor for my PhD, his expertise in memory was invaluable throughout. He helped me to formulate ideas around the methodological design of the recognition bias task employed in this thesis, and always offered support and guidance pertaining to data analysis. Paul also reviewed each chapter of my thesis and provided constructive feedback particularly on the sections pertaining to Memory, of which I am extremely grateful. Paul is a kind, generous and thoughtful individual and was a key part of a fantastic supervisory team. Thank you, Paul!

The next person that comes to mind is ***Dr Vicki Staples***. When it comes to teaching Vicki is the very definition of '*Gold Standard*'. Vicki was responsible for generating my interest in Health Psychology and it was because of her I undertook a MSc as I knew under her support and guidance, I was in the best hands possible. Under her teaching, I learned more than I thought possible, and thoroughly enjoyed learning about Health Psychology. Aside from

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being a central individual to my academic success to date, and a lecturer with certified ***G.O.A.T*** status, Vicki has gone above and beyond to support me. Over the past four years she has been a great supervisor, offering me words of wisdom and helping me to make complex methodological decisions across various studies reported in this PhD thesis. Without Vicki I would never have thought I'd be able to obtain a master's degree, let alone a PhD – so Vicki, thank you for your excellent teaching, supervision, and support throughout all these years.

I cannot write an acknowledgements section without acknowledging the person who first sparked my interest in the field of Pain – ***Professor James Elander***. During the third year of my Undergraduate Degree, as part of an Addictive Behaviours Module, James delivered a session based on his work relating to Opioid Addiction. His lecture was one of the most interesting, thought-provoking, and exciting sessions I had attended as an Undergraduate student. Inspired by James' session, I opted to focus on Opioids in my assignment and learnt about the Opioid epidemic affecting individuals with chronic pain. Naturally, my interest in chronic pain led me to reading more widely after the completion of the module. I then became captivated by the literature surrounding cognitive biases and pain, which combined my two favourite fields of interest together (Health Psychology and Cognitive Psychology) and ultimately helped me to formulate questions I wanted to explore during postgraduate study. Aside from being a fantastic Professor, James is also an extremely courteous individual whom I respect and admire greatly. Thank you, James.

The five individuals named above have arguably had the greatest contribution to my academic career to date. However, there are a few other individuals I would also like to thank below.

I would like to extend my appreciation to ***Dr Jane Montague***. During my PhD, Jane provided me with the opportunity to become an Associate Lecturer and provided me with enough teaching hours to ensure I could still pay my bills and live comfortably whilst studying my PhD. Jane has been a fantastic and supportive boss. Jane also was central to the procurement of some of the equipment used in my PhD research – including new state-of-the-art EyeLink eye-tracking equipment and an accompanying high-spec display monitor. Thank you, Jane - you're awesome!

I would also like to thank the Psychology Technicians, namely, ***Dave Alston*** and ***Rob Morton***. Dave has provided help and support to me over several projects throughout my

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academic career – including the development of a dot-probe task for my Undergraduate dissertation and help with various eye-tracking tasks during my MSc. Thank you, Dave, these projects would not have been possible without your help, support and expertise. Rob has also supported me on numerous occasions, providing me with eye-tracking demonstrations during my Undergraduate degree and helped me to conduct a Risk Assessment for using the Cold-Pressor in my PhD, of which I am extremely grateful. I should also note that it was Dave and Rob who set up the Cold-Pressor (often early in the morning), and ensured it was at the correct temperature prior to me collecting data. I hope you both realise that without you this work would not have been possible – you both are an asset to the University, thank you.

Next, I would like to express my sincere gratitude to all the ***participants*** who took part in the four studies presented in this PhD thesis, and especially thank those individuals who took part with chronic pain. Your contribution has been extremely valuable. I will continue to devote my time to researching the factors that contribute to the development and maintenance of chronic pain, with the hope that my work may one day help to better your lives, and any other lives with which it causes suffering. Given nearly half of the UK population suffer from some form of chronic pain, action is needed now.

Relatedly, I would also like to thank ***Dr Caroline Scott*****,** and her team at the Pain Management Clinic at Derby Royal Hospital for allowing me to shadow the delivery of a 10-week Pain Management Intervention. During my shadowing I was able to share some of my research, interact with patients, but most importantly hear their own personal experiences associated with living with pain which were both inspirational and emotional. I remember many of the patients fondly and would also like to dedicate this thesis to them. I thank them for welcoming me, trusting me enough to share their own personal experiences, and for helping to affirm that it is this area of research I wish to dedicate my career to.

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Chapter 1 **Introduction**

The focus of this thesis is to explore the role of cognitive biases (attention, interpretation, and memory) in non-pain, acute and chronic pain populations. This chapter will begin by outlining the prevalence, impact, and cost of chronic pain in the United Kingdom. Next, a brief overview of pain will be provided, both as an evolutionarily adaptive and maladaptive function. Following this, the four main types of pain will be discussed and classified into two distinct categories: acute and chronic pain. An overview of theoretical approaches to understanding chronic pain will then be presented. Cognitive-affective models of pain will then be discussed followed by the three main forms of cognitive bias, namely, attentional bias, interpretation bias and memory bias. Reasons for, and the implications of, investigating cognitive biases in pain in the present thesis will then be proposed, with the chapter culminating with an outlining of aims and objectives of the PhD research.

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1.1 Chronic Pain in Adults - a major public health issue

1.1.1 The Prevalence, Cost, and Impact of Chronic Pain in the United Kingdom

Pain is defined as an *"aversive sensory and emotional experience typically caused by, or resembling that cause by, actual or potential tissue injury"* (The International Association of the Study of Pain, IASP, cited in Raja et al., 2020). Healthcare professionals typically distinguish between three different types of pain. To expand, pain that is short in duration (< 12 weeks) is described as 'acute pain', pain that is long in duration (> 12 weeks) is described as 'chronic pain' and pain that comes and goes is described as 'intermittent pain'. Chronic pain is the most complex form of pain and is often difficult to treat (Weisberg & Clavel, 1999). A recent systematic review and meta-analysis pooled data from 7 studies to provide accurate and contemporary national estimates of chronic pain (Fayaz et al., 2016). They found the prevalence of chronic pain in the United Kingdom (UK) to range from 35-50%, with 10.4% to 14.3% of these individuals experiencing pain that is moderately to severely disabling. Chronic pain is most common in women, older people and those from a lower socio-economic background (Van Hecke et al., 2013). As the average age of the population continues to rise in the UK, with 18% currently aged 65 or over and 2.4% aged 85 and over, the incidence of chronic pain is expected to rise significantly (Office for National Statistics, 2017). Indeed, changes in lifestyle factors are likely to also increase the prevalence of conditions associated with chronic pain. For example, by 2030 the UK population is predicted to be 35% less active than in the 1960s, with 48% of men and 43% of women obese by that date (National Health Service, 2011; Public Health England, 2019).

On a national level, chronic pain exerts an enormous economic burden, with back pain alone estimated to directly cost the UK economy £1.6*bn* (Maniadakis & Gray, 2000). This is perhaps unsurprising given that low back pain is the leading cause of disability worldwide (Wu et al., 2019). Further, primary care management of patients with chronic pain accounts for 4.6 million appointments annually in the UK, equivalent to 793 full-time general practitioners, at a cost of approximately £69*m* (Belsey, 2002). Significant productivity costs have also been reported, with pain patients losing 41% of the total number of work hours available and missing 19.4% of their time employed as compared to those not suffering from pain (Kronborg et al.,

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2009). Indeed, from 1999-2000, arthritis was responsible for 206 million working days lost in the UK alone, equivalent to a loss of production of £18*bn* and a direct cost to UK health and social services of £5.5*bn* (Arthritis Care, cited in Phillips, 2006).

Chronic pain also has a profound physical, psychological, and social impact. A multi-national study examined the prevalence and impact of persistent pain among primary care patients from 15 centres in Asia, Africa, Europe and the Americas. Persistent pain sufferers were more likely to suffer from psychological disorders including anxiety and depression, experience limitations to their physical activity, and possess unfavourable health perceptions (Gureje et al., 1998). Moreover, Castro et al. (2009) assessed the frequency of psychiatric disorders in 400 patients attending a Pain Clinic in Brazil. Of this sample, 42% experienced depressive episodes, 54% dysthymia, 36.5% social phobia, 8.5% agoraphobia and 7.3% panic disorder. Hence, psychiatric and medical pathologies often interact in pain patients. Pain also impacts marital partnerships, with individuals reporting increased marital conflict, role tension and reduced sexual satisfaction (Flor et al., 1987; Snelling, 1994). Considering the family unit more generally, pain is cited as the main cause of changes to leisure activities (Ojeda et al., 2014).

As a consequence of the above, an increasing number of researchers are trying to understand the psychological factors which may contribute to the aetiology and maintenance of chronic pain, from neuroscience research focusing on nociception, to cognitive psychologists focusing on mental processes including attention, interpretation and memory biases. The research presented in this thesis was progressed to further understand the role of attention, interpretation and memory biases in non-pain, acute and chronic pain populations, with the hope that these findings can contribute to bettering the lives of adults suffering with pain.

1.1.2 Pain as an adaptive function

Although unpleasant, pain serves as an evolutionarily adaptive function by capturing attention, interrupting behaviour, and urging an organism to instinctively react (Eccleston & Crombez, 1999). From a neurological perspective, pain can take multiple forms. For instance, pain that arises from actual or threatened damage to non-neural tissue because of the activation of

peripheral nociceptive fibres is classified as 'nociceptive pain' (Zaki et al., 2016). Nociceptive pain is triggered by a high threshold sensory neuron (i.e., a nociceptor) that activates in the presence of intense stimuli (Basbaum et al., 2009). It serves as an early-warning physiological protective system that aids an organism's survival by detecting and minimising contact with the source of the noxious stimulus (Woolf, 2010). Homeostatic modalities that aid survival include interoceptive sensations such as temperature (i.e., removing our hand away from something we perceive to be too hot or cold), itch (i.e., removing irritating objects and agents that assault the skin and consequently the body's integrity such as insects, sharp objects, allergens) and muscle ache (i.e., highlighting potential tissue damage; Paus et al., 2006; Woolf, 2010). This has led some researchers to describe pain as a 'homeostatic emotion' comprising both sensation and motivation (Craig, 2003; Appelhans & Luecken, 2008; Jensen & Finnerup, 2009). It is, therefore, not surprising that nociceptive pain demands immediate attention and action to fulfil its protective role (Van Damme et al., 2010). Protection can transpire through numerous means including the nociceptive flexion reflex it effectuates (Skljarevski & Ramadan, 2002), the unpleasantness of the sensation elicited, and the emotional suffering it provokes (Lee & Tracey, 2010).

Pain associated with actual tissue damage whereby cytokines are produced to facilitate inflammation is commonly described as 'inflammatory pain' (Zhang, & An, 2007). Like nociceptive pain, inflammatory pain is also considered to be both adaptive and protective (Woolf, 2010). This is because pain hypersensitivity (an exaggerated and prolonged pain response) occurs following tissue damage, which discourages physical movement and contact, subsequently aiding the healing process of the injured body part (Woolf, 1983). For instance, following a surgical procedure, the tenderness of the surgical wound serves to reduce further risk of damage and promote recovery. In such circumstances, normally benign sensations now elicit pain (Bechert & Abraham, 2009). Typically, once the initial tissue injury has healed, the associated inflammatory pain ceases to exist. That said, while inflammatory pain is adaptive, patients who experience ongoing inflammation as with ankylosing spondylitis, gout and rheumatoid arthritis, need to have their pain managed, as pain will persist for as long as inflammation is active (Costigan et al., 2009).

1.1.3 Pain as a maladaptive function

While the above examples highlight forms of pain that have an adaptive function, there are also forms of pain that serve no biological function (i.e., are maladaptive). This pain type is commonly described as 'pathological pain'. Woolf (2010, pg. 3742) provides the following analogy to describe the characteristics of pathological pain… *"If pain were a fire alarm, the nociceptive type would be activated appropriately only by the presence of intense heat, inflammatory pain would be activated by warm temperatures, and pathological pain would be a false alarm caused by malfunction of the system itself"*. One form of pathological pain results from abnormal functioning of the peripheral nerve, the dorsal root ganglion, or the central nervous system, and causes significant suffering and distress (Woolf & Mannion, 1999). This type of pain is commonly classified as 'neuropathic pain'. Neuropathic pain syndromes tend to have clinical characteristics including negative symptoms (i.e., loss of function in the somatosensory system), such as pain in an area of partial or complete sensory loss, and positive symptoms (i.e., gain of function in the somatosensory system), including allodynia (i.e., hypersensivity to non-noxious stimuli e.g., a feather touch), hyperalgesia (exaggerated response from a noxious stimulus), paraesthesia (abnormal tingling e.g. 'pins and needles'), dysaesthesia (unpleasant sensation felt upon touch), and pain (Jensen & Finnerup, 2014). Fayaz et al. (2016) found the prevalence of chronic neuropathic pain to range from 8.2% to 8.9%. This is important as patients suffering from neuropathic pain often report intense, long-lasting pain and a reduced quality of life (Haanpää et al., 2009).

Although neuropathic pain stems from abnormal functioning of the nervous system, pain can also occur in conditions where there is no identifiable noxious stimulus, inflammation, or damage to the central nervous system. This form of pain is often described as 'dysfunctional pain' and like neuropathic pain neither protects nor facilitates healing or repair. Thus, dysfunctional pain is considered maladaptive, potentially persistent and a disease state in its own right (Costigan et al., 2009). Dysfunctional pain shares some clinical features of neuropathic pain including hyperalgesia and abnormal sensory processing and is associated with a variety of clinical disorders, including fibromyalgia, irritable bowel syndrome (IBS), and phantom limb pain (Jensen & Finnerup, 2009; Sumitani et al., 2010). Given the complex nature of this form of pain, little research has attempted to explore the pathophysiological mechanisms which may be responsible for it (Nagakura, 2015). However, the urgency for

identifying the aetiology of dysfunctional pain is likely to continue to rise, considering its increasing prevalence amongst general populations for chronic pain conditions, including fibromyalgia (2-8%) and IBS (7-21%, Clauw, 2014; Chey et al., 2015; Davis et al., 2014; Nagakura, 2015), the negative psychological effects having to live with inexplicable pain causes, its detrimental impact on quality of life (Sarzi-Puttini et al., 2012), the lack of effective therapies available, and the expensive associated healthcare costs (Nagakura, 2015).

1.1.4 Acute versus Chronic Pain

Considering the four main types of pain discussed above (i.e., nociceptive, inflammatory, pathological, dysfunctional), each can be further classified into two distinct categories, these are 'acute' and 'chronic' pain. Acute pain, defined as "*the normal, predicted physiological response to an adverse chemical, thermal or mechanical stimulus, associated with surgery, trauma and acute illness"* (Carr & Goudas, 1999), is elicited by damage to body tissue and the activation of nociceptive transducers at the site of damage. Acute pain is generally agreed to last for a few days or at most 12 weeks (Zeller et al., 2008).

Two major forms of pain can be categorised as acute, these include nociceptive pain and inflammatory pain (provided inflammation is not persistent). A key distinction between acute and chronic pain is that in acute pain the injury does not overwhelm the body's reparative mechanisms, which allows the process of healing to occur without medical intervention (Loeser & Melzack, 1999). That said, medical interventions are important in acute pain and are commonly sought by patients (Shi et al., 2007). This is because medical interventions can help to manage acute pain and accelerate the healing process by shortening the duration of injury. Once healing has been completed acute pain stops.

Pain that continues to persist beyond this time (i.e., 12 weeks) is not classified as acute pain but chronic pain (Treede et al., 2015). It is crucial to recognise that there are mechanisms by which acute pain can transform into chronic pain. To expand, following tissue damage, nociceptive pain is often accompanied by inflammatory, visceral, and neuropathic pain mechanisms. This can lead to sensitisation of the nervous system which heightens and maintains pain, thus explaining why in some cases an individual's acute pain can become chronic (Feizerfan, 2014). Indeed, psychological variables including depression, anxiety, pain

beliefs, catastrophising and coping behaviour have all been found to moderate the transition from acute to chronic pain (Fransen et al., 2002; Pincus et al., 2002; Katz & Seltzer, 2009).

Pain that persists beyond normal tissue healing time, generally agreed to be 12 weeks, is commonly described as 'chronic pain'. To recap, there are three main pain states that can be classified as 'chronic'. These include (persistent) inflammatory pain, pathological pain, and dysfunctional pain. Irrespective of its aetiology, chronic pain has been found to contribute to substantial disability and a poorer quality of life among patients, restricting one's ability to sleep, exercise, do household chores and maintain relationships with friends and family (Matos, Bernardes & Goubert, 2016; Peters et al., 2017; Harvold et al., 2018). Importantly, it is now widely acknowledged that mood disorders, such as anxiety and depression, play a key role in the exacerbation of pain perception (Woo, 2012). Hence, pain has a strong psychological component.

There are a multitude of different forms of chronic pain, including chronic back pain, chronic headache, and fibromyalgia, many of which are commonly triggered by injury or disease. Unlike acute pain, chronic pain overwhelms the body's reparative mechanisms due to the extensiveness of the trauma, scarring, or as a result of damage to the nervous system which prevents it from restoring itself back to a normal state (Loeser & Melzack, 1999). All forms of chronic pain lead people to seek healthcare. For instance, it is estimated that pain-related problems account for up to 80% of visits to physicians (Voscopoulos & Lema, 2010). Indeed, given that 40% (or more) of patients in routine practice settings fail to receive adequate pain relief, chronic pain is now considered a major public health issue (Glajchen, 2001).

Due to the unrelenting nature of chronic pain, it is now widely acknowledged that this disease should be treated using a holistic approach. A multidisciplinary approach is also needed for the development of pain management interventions. While treatments for chronic pain are unable to resolve underlying pathology, tackling the associated psychological processes that accompany the chronic pain experience may help to improve patients' subjective experience of pain, the subsequent management of their pain and their quality of life.

1.1.5 Definitions of 'Pain' – prioritising simplicity over validity and utility?

It is important to note that whilst the definitions of Pain outlined above include either a temporal dimension (e.g., acute vs chronic pain) or attempt to distinguish between pain where tissue damage is present or absent, acknowledgement should be made concerning the extent to which these definitions accurately apply to individuals with pain and how useful such definitions are. This will now be discussed briefly below.

One common feature of pain-related definitions is based on the temporality of pain duration. As previously mentioned, Acute Pain is proposed to last for a short duration (< 12 weeks), while Chronic Pain is proposed to last for a long duration (> 12 weeks). However, these categorisations of pain can be criticised as overly simplistic and inadequate, given their inability to encapsulate specific types of pain, for example, menstrual pain. While menstrual pain is a common (and normal) part of a woman's menstrual cycle (NHS, 2022), pain generally lasts for between 28-72 hours. Hence this form of pain could be categorised as 'acute'. However, given menstruation occurs on a cyclical basis (every 28 days or so), its monthly re-occurrence shows that it persists well beyond three months. Thus, a key question remains, can menstrual pain be categorised temporally as a form of acute or chronic pain?

Other definitions of pain, such as 'dysfunctional' pain are not devoid of scrutiny either. To recap, dysfunctional pain is defined as 'pain that occurs in conditions where there is no identifiable noxious stimulus, inflammation, or damage to the central nervous system'. However, the term 'dysfunctional' is pejorative and lacks specificity, indicating abnormality or impairment. Evidence suggests that dysfunctional pain is generally viewed as an undesirable attribute of chronic pain, with such individuals experiencing considerable stigma (Van Alboom et al., 2021). Such descriptors can engender negative reactions in others and/or contribute to a misinformed view that the individual is somehow flawed or undesirable. Whether this is due to the uncertainty regarding the nature of the pain, the high rates of treatment failure, perceived 'excessive' utilisation of health services, and/or patient-clinician interactions (e.g., disbelief, stereotypes) remains to be fully understood (Lloyd et al., 2020).

Indeed, research suggests that when no clear explanation as to the origin of pain can be identified, ambiguous psychopathological interpretations of an individual's condition can occur (Arnaudo, 2021). This may lead to negative attitudes among health professionals

including suspicion of deception, less sympathy, disliking patients and even being less inclined to help when the pain is acute or when tissue pathology is found (De Ruddere & Craig, 2016). Equally as important is the potential implications of such definitions to a patients' sense of self – with a lack of a clear diagnosis contributing to scepticism about the nature and reality of their own symptoms, potentially leading to individual's questioning the credibility of their own pain (Werner & Malterud, 2003).

Stigmatisation is also likely to occur with the use of definitions such as 'psychogenic pain'. Here, the term 'psychogenic' may be incorrectly assumed to be consistent with 'imaginary' or 'unreal' pain. As stated previously, no isomorphic relationship exists between pain and tissue damage. Considerable evidence challenges the view that pain is a trustworthy marker of disease existence. This has resulted in calls for pain to be viewed as a disease state in its own right (Raffaeli & Arnaudo, 2017). The distinction between differing types of pain such as 'psychogenic' and 'neuropathic' pain provide a metaphorical contrast between 'unreal' and 'real' pain – inadvertently implying that real pain is physical in nature, can be detected, and the patient is not responsible for its onset and maintenance. In contrast, pain that cannot be connected to physical anatomy implies the pain is 'unreal' due to the non-physical nature of its causes. This may then lead to the assumption that the individual is responsible for the onset and maintenance of their pain (Covington, 2000).

Considering all of the above, whilst the standard definitions of pain have been included within this PhD thesis, it is important to acknowledge that these definitions are not without criticism. Most definitions that exist to date are not able to fully encapsulate individuals living with varied types of pain. Additionally, terms such as 'dysfunctional' and 'psychogenic' are outdated, have no utility and are likely to have a range of negative implications, including both blame and stigma for individuals with pain. To be able to better represent people living with varied types of pain it is important that definitions move away from focusing on underlying pathology, and instead offer a more informed biopsychosocial perspective. Relatedly, the historical and modern approaches to understanding pain will be outlined in the next section of this PhD thesis.

1.2 Historical and Modern Approaches to Understanding Pain

Historically, numerous explanations have been proposed to try and explain pain. Early models of pain described it within a biomedical framework, arguing that pain is the result of biological pathology. For instance, Rene Descartes (1956 – 1650) described a direct pathway from the source of the pain in the body to an area of the brain that detects the painful sensation. Goldschneider's (1920) pattern theory of pain extended this, asserting that following damage to an area of the body, nerve impulses determine the degree of pain and send messages from the damaged area directly to the brain. Von Frey's (1985) specificity theory of pain later proposed that specific pain receptors (i.e., mechanoreceptors) transmit signals to a 'pain centre' in the brain that produces the perception of pain (Moayedi & Davis, 2012). A key limitation to each of these explanations is the lack of acknowledgement of other factors that influence pain – namely, psychological, and socio-environmental factors.

Modern explanations of pain have increasingly placed emphasis on psychological and socio-environmental factors. To expand, Melzack and Wall's (1965) Gate Control theory (GCT) of pain combines key concepts from Von Frey's specificity theory and Goldschneider's pattern theory to postulate that 'pain messages' travel from the periphery of the body through nerve 'gates' in the spinal dorsal horn and up to the brain. In some instances, these pain messages are passed along more readily resulting in a more intense pain experience (gate open), whereas in other instances pain messages are passed less readily or are prevented from reaching the brain at all (gate closed). However, GCT goes beyond the biomedical explanations by describing pain as a perception and experience as opposed to just a sensation. Pain is viewed as an active process with the individual interpreting and appraising the painful stimulus. Indeed, this theory also acknowledges that many factors are involved in pain perception and that there is not just a singular physical cause. Consequently, GCT is often credited for revolutionising the way in which pain is viewed today, sparking the development of new perspectives on pain. It has also been credited as the first theory to integrate physiological and psychological mechanisms of pain within the context of a single model (Dickenson, 2002; Moayedi & Davies, 2013).

1.2.1 The Biomedical Model and Limitations

Traditional biomedicine views pain as a symptom reflecting physical injury or disease process. Consequently, diagnosis and treatment tend to predominantly focus on the underlying tissue damage and neglects the pain itself. According to the biomedical view, once treatment and/or natural healing occurs the pain will disappear. While this assumption is often the case with acute pain, such as a surgical wound or broken limb, it is unfitting for patients with chronic, persistent and unrelenting pain which sometimes occurs in the absence of underlying pathology (Foster et al., 2003). Indeed, amputees' experiences of 'phantom limb pain' present challenges for proponents of the biomedical approach. It is believed that the first medical description of pain following amputation of a body part was given by a French military surgeon named Amroise Pareé (1510 – 1590). Following amputation, he reported that patients complained of severe pain in the missing limb (e.g., arm, leg) long after amputation. Silas Weir Mitchell later coined the term 'phantom limb syndrome' in 1871 (Nathanson, 1988). It is estimated that 80% of individuals who undergo amputation feel pain in the amputated limb that no longer exists, despite lacking a peripheral basis, and that this pain continues long after the area of amputation has healed and may last for the rest of an individual's life (Flor, 2002). Such statistics clearly highlight the inadequacy of the biomedical approach, with the above example potentially indicating a role for psychological factors in the experience of pain (Gamsa, 1994; Turk & Okifuji, 2002). The biomedical model is therefore not sufficient to meet the needs of patients with chronic pain. Rather than viewing chronic pain as merely a symptom, it should be treated as a disease state in its own right. Thus, when underlying pathophysiology cannot be treated, focus should shift to the pain itself and the effects of the pain on the sufferer. As a consequence of the shortcomings of the biomedical approach, alternative conceptualisations of chronic pain have arisen, including that of the now predominant biopsychosocial model (Engel, 1977).

1.2.2 Integration of Psychological and Socio-environmental factors via the Biopsychosocial Model

While the traditional biomedical approach holds a dualistic viewpoint, proposing that the mind and body are two distinct entities that operate independently of one-another, the inadequacies

of this model have contributed greatly to a growing recognition that psychosocial factors (e.g., anxiety, depression, stress, cognitive distortions) can be partly responsible for the development of a chronic pain condition, prolonging the pain syndrome and influencing a patient's response to medical treatment. In 1977, George Engel called for a new approach that avoided the pitfalls of the biomedical model which had since dominated the field of medicine. Engel's call for a new approach ultimately led to the growth of disciplines such as behavioural medicine and health psychology (Gatchel et al., 2007). This, in turn, triggered the development and evolution of the biopsychosocial model, which has been particularly influential in the field of chronic pain.

As mentioned previously, Melzack and Wall's GCT helped to formulate new perspectives of pain, including the biopsychosocial model (Engel, 1977). One of the key advantages of GCT is that it is a sensory-affective interactive theory, acknowledging that other factors (e.g., cognition) can contribute as causal and maintenance factors to the experience of pain. This has led to a key distinction between *nociception* and *pain*. To expand, nociception is defined as *"the detection of potentially tissue-damaging thermal or mechanical energy by specialised nerve endings"* (Loeser & Fordyce, 1983, pp.332). Pain, on the other hand, is a subjective perceptual process that results from the transduction, transmission, and modulation of sensory input from one's internal and/or external environment. Pain is the product of higher brain processing in the cerebral cortex and thalamus and is thus influenced by other emotions, such as anger, anxiety, and depression (Gatchel, 2007). Consequently, it is unsuitable to make links between the degree of nociceptive input and one's level of pain, as the brain processes nociceptive signals and translates them into a subjective experience (Mackey & Maeda, 2004). Hence, an isomorphic relationship does not exist between tissue damage, nociception, and one's reported level of pain.

The biopsychosocial model attempts to provide a comprehensive overview of the many mechanisms involved in the processing of pain. This model asserts that biological (e.g., tissue damage), psychological (e.g., emotions, cognitions, behaviours) and social factors (e.g., work, relationships) all contribute to the experience of pain and the aetiology of chronic pain. Consequently, significant research has been dedicated towards investigating the psychological factors that may influence the experience of pain, including subjective-affective cognitive

processes (e.g., attention, self-efficacy, catastrophizing) and behavioural processes (e.g., facial/audible pain expressions, avoidance of physical activity, negative affect).

1.3 Cognitive-Affective Models of Pain

To recap, the IASP (cited in Raja et al., 2020) defines pain as an "*aversive sensory and emotional experience typically caused by, or resembling that caused by, actual or potential tissue injury*". This definition takes a biopsychosocial view of pain, acknowledging the importance of emotional factors. Consequently, much research has been dedicated to investigating the cognitive and affective factors that influence pain. For instance, it is well documented that chronic pain patients display anger, fear and avoidance behaviours (Trost et al., 2014; Crombez et al., 1999; Asmundson et al., 1999), mood disorders including anxiety and depression (Benjamin et al., 2000), and tend to feel helpless (Samwel et al., 2006), ruminate (Edwards et al., 2011) and magnify their thoughts and feelings towards the painful situation (i.e., catastrophise, Severeijins et al., 2001). Hence, it is unsurprising that cognitive-affective factors modulate the experience of pain and influence pain outcomes (e.g., disability). In this section an overview of cognitive-affective models of pain are presented, for which a specific role is implicated for cognitive biases in the aetiology and maintenance of chronic pain.

1.3.1 The Fear Avoidance and Cognitive-Affective Model's of Pain

The Fear Avoidance Model (Vlaeyen & Linton, 2000) – arguably one of the most influential models of pain - proposes that at the heart of pain chronicity are anxiety-related factors which include fear and avoidance. To expand, the way in which pain is interpreted (either threatening or non-threatening) may lead to the development of chronic pain and disability. The model asserts that when acute pain is interpreted as non-threatening individuals display low or no fear of pain and return to a normal state of functioning after a period of recovery. However, if acute pain is interpreted as threatening a viscous cycle may ensue, which involves individuals catastrophising about pain, resulting in the development of pain-related fear pertaining to movement and (re)injury, avoidance of activity and subsequent hypervigilance to pain. This hypervigilance fuels escape-avoidance tendencies which contribute to disease, disability, and

depression. While such behaviour may be adaptive in the acute pain stage (i.e., to promote recovery), in instances of long-term pain the opposite effect is observed. In some extreme cases avoidance of physical activity can lead to physical deconditioning/disuse syndrome, which reduces the threshold at which subsequent pain is experienced (Bortz II, 1984). This is important as it contributes to further disability, subsequently reinforcing the sequence of the vicious cycle.

The claims of the FAMP have received much empirical support. Correlational studies have revealed that pain catastrophising and pain-related fear are important predictors of present pain injury and disability (Peters, Vlaeyen & Weber, 2005); that pain patients who catastrophise about pain report more pain intensity, increased perceived disability and experience more psychological distress (Severeijins et al., 2001); and that catastrophising is significantly associated with negative mood, increased pain and a reduction in the weight lifted in individuals prior to a first exercise bout (Sullivan et al., 2002). Prospective research has also revealed that pain-related fear predicts subsequent disability and participation in physical activity in patients with acute lower back pain (Swinkels-Meewisse et al., 2006). Additionally, fear-avoidance beliefs have been found to be a prognostic factor for poor work-related outcomes (i.e., absence from work, number of sick days) in patients with sub-acute lower back pain (see Wertli et al., 2014 for review). Most recently, a systematic review of cross-sectional and longitudinal studies examining pain catastrophising, pain intensity and disability in individuals with chronic musculoskeletal pain, found that higher levels of pain catastrophising were frequently found to be associated with, and prospectively predict, chronic pain intensity and disability (Luque-Suarez et al., 2019). That said, given the 'very low' quality of evidence used and the large heterogeneity because of conducting multiple meta-analyses, the findings of this review should be interpreted with caution.

1.3.2 Cognitive-Affective Model of the Interruptive Function of Pain

At roughly the same time, Eccleston and Crombez (1999) developed the Cognitive-Affective Model of the Interruptive Function of pain. This model proposes three key principles; i) attention is a mechanism of selection for action where pain is selected for escape, ii) pain is ontogenetically and evolutionarily predisposed to interrupt attention to limit the impact of

aversive events and iii) a number of variables moderate the interruption of pain into awareness, including; threat, pain intensity, novelty, predictability, catastrophising, somatic awareness and factors relevant to the environment of pain (e.g., task difficulty, emotional arousal). Like the FAMP, research has provided evidence for the key tenets of this theory. Pain intensity has been shown to interfere with task performance in healthy and chronic pain patients (Eccleston, 1994; Van Ryckeghem et al., 2013). Novelty has been shown to capture attentional resources more easily (Legrain et al., 2005); and greater disruptions of task performance have been observed in high-threat situations and in those who catastrophise about pain (Crombez et al., 1998a, Moseley et al., 2003).

1.3.3 The Schema Enmeshment Model of Pain

Following a review of cognitive biases in chronic pain, Pincus and Morley (2001) developed the Schema Enmeshment Model of Pain (SEMP). This model proposes three schemas, representing pain (i.e., the sensory features), illness (i.e., affective and behavioural consequences of illness), and the self (i.e., a multi-factorial structure including evaluation of self-worth). Pincus and Morley (2001) assert that 'enmeshment' occurs when the three schemas intersect, which causes affective distress and psychological problems (e.g., depression), which then further exacerbate the chronic pain condition. Indeed, these schemas are proposed to always overlap to an extent, hence, factors including the level of enmeshment, content of the schemas and the timing/content of enmeshment are important. For instance, they propose that pain patients with concurrent distress and depression exhibit greater enmeshment of the self and pain schema, such that patients associate pain as integral to the self (i.e., a part of their identity) which in turn causes suffering and distress. That said, Pincus and Morley (2001) acknowledge that this was a post-hoc explanation for the observed data in their review and offered no independent way of assessing the degree of enmeshment.

Subsequent research by Read and Pincus (2004) found that that depressed patients with Chronic Low Back Pain (CLBP) were more likely to recall ill-health related adjectives in the current condition and not in the future-referent condition. Whereas a non-depressed LBP group and healthy controls showed no differences in recall of ill-health or depression words in either the current/future-referent condition. Consequently, the authors asserted that negative future

thinking may not necessarily be an important feature in chronic pain patients with depressive symptoms compared to their depressive symptom without pain counterparts. Van Ryckeghem et al. (2013) aimed to test the strength of the association between pain and self-schema using an Implicit Association Test. Results showed that the pain and self-schema were more strongly associated in patients with chronic pain than in healthy controls. Furthermore, participants with chronic pain exhibited a stronger association between self and pain schema, and this was related to a heightened level of pain severity, suffering, anxiety, and helplessness.

1.3.4 The Misdirected Problem-Solving Model

To build upon previous theories including the FAMP, Eccleston and Crombez (2007) later proposed the Misdirected Problem-Solving Model (MPSM) which views pain patients as active problem solvers situated in a world dominated by multiple threats. The fundamental belief of this model is that chronic pain patients live in the context of enduring pain which interrupts attention, fuels worry about the causes and consequences of pain with reference to the self and others and causes hypervigilance to pain. This model asserts that pain is often viewed by patients using a 'biomedical problem frame' which is characterised by patients attempting to find solutions focused on the removal of pain. If such problem-solving attempts are successful, pain and worry subside. However, in situations where the problem-solving attempts are not successful, worry is fuelled which results in the development of a 'perseverance loop'. This loop occurs when the failure to find an adequate solution to the problem of pain amplifies worry, which in turn strengthens motivation to persevere and solve the problem. However, this perseverance is unlikely to achieve a positive outcome if individuals continue to tackle pain using a biomedical problem frame when no biomedical solutions are available. Hence, adopting a different problem frame, for example, by channelling existing problem-solving efforts towards the attainment of functional goals, may provide a more adaptive solution. Considering the above, the MPSM assigns a causal role to cognitive-behavioural factors (i.e., beliefs about the cause of pain, attention, worry, problem-solving) in the maintenance of chronic pain. Thus, highlighting the importance of cognitive biases, most notably attentional bias, which is proposed to fuel subsequent worry and hypervigilance to pain. Therefore, further understanding of said attentional bias is warranted to gain a detailed insight into the chronic pain experience and to promote more adaptive pain outcomes.

Research by Flink et al. (2012) examined the links between catastrophizing, problem-framing and problem-solving behaviour in a general population sample with perceived problems with spinal pain. Catastrophising and problem-solving were assessed on first occasion and healthcare seeking was assessed 7 months later. Results supported the concepts outlined in the MPSM, but the direction of the relationships were found to be more in line with the predictions of the FAMP. To expand, catastrophizing was found to mediate the relationship between biomedical problem-framing and medically oriented problem-solving. This is opposite to the order proposed by the MPSM which predicts that biomedical problem-framing mediates the relationship between catastrophizing and problem-solving behaviours. Instead, the FAMP proposes that pain beliefs (e.g., pain means serious harm and/or injury) or in other terms 'biomedical problem-framing' may result in the development of catastrophising and medically oriented problem-solving. Hence, while Flink et al. (2012) provide evidence to support the concepts included in the MPSM, the data indicates that the direction of the relationships are not in accordance with the predictions of the MPSM which implies refinement of the model may be needed.

1.3.5 The Motivational Account of Attention to Pain

In 2010, Van Damme et al. proposed the Motivational Account of Attention to pain, which asserts that pain is best understood in the context of goal pursuit. The model claims that pain-related information comes into the focus of attention in two ways. First, while pain is often related to the goal being currently pursued, pain is an evolutionarily acquired alarm signal of bodily threat which captures attention and interrupts ongoing goals – much like the proposals of Cognitive-Affective Model of the Interruptive Function of Pain. Thus, pain can interrupt current goal pursuit meaning that goal shielding (i.e., the protection of ongoing goals) is not absolute. Second, individuals may also pursue goals directly relating to pain (e.g., attempting to alleviate or control the pain or searching for an underlying cause that may be responsible for the pain). In circumstances where individuals prioritise pain-related goals, this will be accompanied by an increase in the processing of pain-related information – over other information – in one's environment. Hence, the preferential allocation of attentional resources to pain-related information at the expense of other information could then be conceived as a goal-directed mechanism. The model emphasises that if pain control becomes the focal goal,

individuals will exhibit enhanced attentional processing of pain-related information, which in turn, increases the interruption of pain in daily life.

1.3.6 The Threat Interpretation Model

In recent years, a new theoretical model has been proposed to guide pain-related attentional bias research. The Threat Interpretation Model (TIM, Todd et al., 2015) was developed following a systematic review of the attentional bias and pain outcomes literature. The TIM proposes that the attentional processes displayed are dependent on whether an individual first categorises a stimulus as pain relevant. If not pain relevant, normal attentional processing ensues. If pain relevant, then the attentional processes displayed are determined by the perceived threat of that stimulus. If the stimulus is interpreted as non-threatening, again normal attentional processing follows. However, if interpreted as threatening individuals display a vigilance-avoidance attentional bias, characterised by immediate attentional allocation to threat, followed by rapid disengagement and avoidance (e.g., via the focus on positive stimuli, see **Figure 1**). The TIM also makes theoretical predictions dependent on whether the perceived stimulus threat value is low, moderate, or high. Under conditions of sustained attention, low threat is presumed to lead to easy disengagement of attention, moderate threat to more difficulty disengaging attention, and high threat to attentional avoidance.

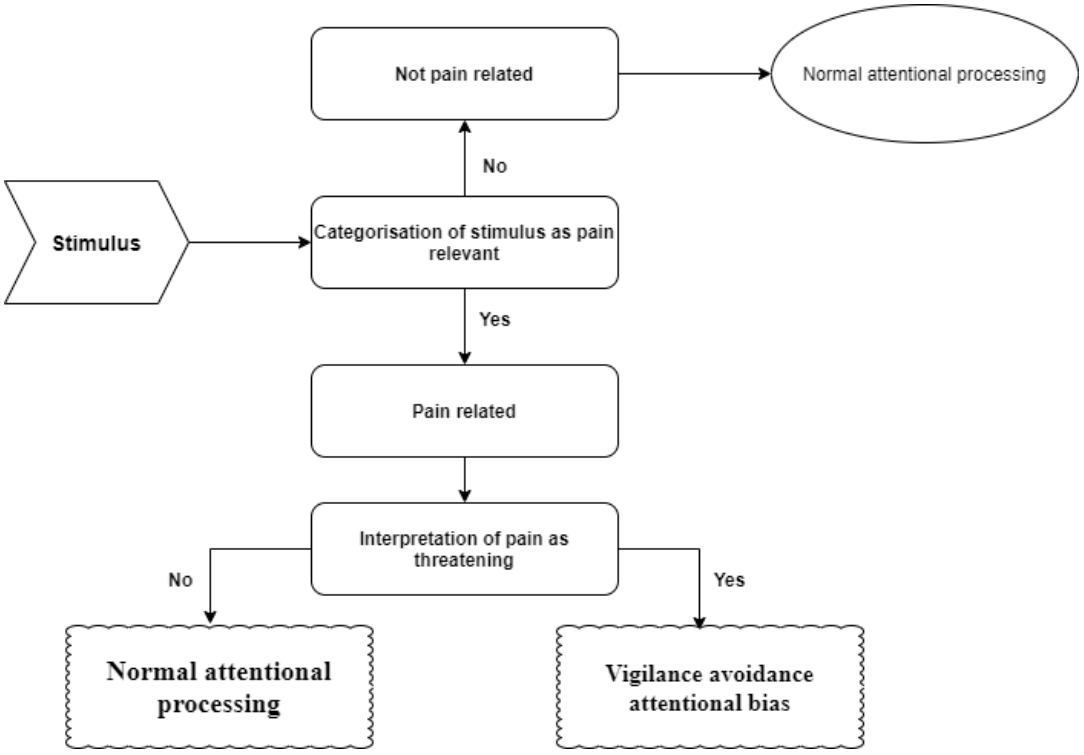


Figure 1.1: **The Threat Interpretation Model of Attentional Biases to Pain**

To date, the TIM has received mixed evidence for its claims. Early support for the model was engendered by Brookes et al. (2017) who examined the effects of manipulating rumination on attentional processes in an acute experimental pain task in a healthy sample of undergraduate students. Participants were randomly allocated to a rumination condition where participants were presented with threatening information regarding an upcoming cold-pressor task, or a distractor condition which involved participants thinking about physical aspects of their bodies unrelated to the cold-pressor task. Participants then completed a dot-probe task which involved the presentation of neutral, affective, and sensory word-pairs on a computer screen (one left, one right) for two durations, 500ms (to measure early attention) and 1250ms (to measure late attention). After this time, a visual probe appeared on the screen (in the location of one former word) and participants were required to identify the location of the probe (left or right). Speeded responses to trials whereby the probe appears in the former location of the pain-word is indicative of vigilance, whereas delayed responses are indicative of avoidance (a more detailed overview of the visual-probe task is presented in Chapter 2). Consistent with the predictions of the TIM, a vigilance-avoidance pattern of processing was observed for affective

pain words. To expand, participants responded faster to probes replacing affective pain words during early orientation (500ms), and delayed responses to trials whereby the probe replaced the affective pain words during later orientation (1250ms). Thus, Brookes et al (2017) concluded that a vigilance-avoidance pattern of processing occurs following rumination manipulation.

Like the procedure of Brookes et al. (2017), Sharpe et al. (2017) randomly allocated undergraduate students to a threatening condition or a reassuring condition whereby participants received corresponding information about an upcoming cold-pressor task, and then divided participants into 'high' and 'low' fear of pain groups. Participants then completed a dot-probe task used in conjunction with eye-tracking technology. Results showed that participants who received threatening information were less likely to direct their first fixation on the pain words, particularly the affective pain words. Moreover, the individuals in the high-threat group that did fixate on affective pain words, did so more quickly than for sensory pain words, again supporting the notion of a vigilance-avoidance pattern of processing. Regression analyses revealed that initial vigilance towards affective pain words influenced participants pain outcomes, with high-threat participants experiencing a reduced pain threshold. Taken together, the above findings suggest that presenting individuals with highly threatening information regarding an upcoming painful procedure can induce a vigilance-avoidance pattern of processing and influences ones' subjective experience of pain. Thus, both studies are consistent with predictions of the TIM.

However, Todd et al. (2016) found mixed evidence for the TIM in healthy participants. Similar to the methodology of Brookes et al., (2017) participants were presented with threatening or reassuring information about an upcoming cold-pressor task, prior to completing an attentional bias (dot-probe) and interpretation bias (incidental learning) task whilst eye-movements recorded. Consistent with the TIM, threat was found to be associated with difficulty disengaging from painful facial expressions. However, threat did not influence early attentional processing, providing no evidence of hypervigilance during initial orienting. Hence, Todd et al. (2016) concluded that cognitive processing biases may only occur in clinical samples and that further research is needed to understand the precise nature of these biases.

Nonetheless, it is important to acknowledge that the above studies tended not to measure cognitive biases both *prior to* and *after* experience to pain. This is particularly important otherwise one is unable to assess whether the pain experience itself influences cognitive processing. Consequently, it is difficult to assess if, and how, pain shapes cognitive biases including attention and interpretation. Thus, laboratory work inducing pain in healthy participants may prove invaluable in furthering understanding of the dynamics between cognitive biases and pain and if/how they change prior to pain experience vs. after pain experience.

1.3.7 The Integrated Functional-Contextual Framework

Most recently, Van Ryckeghem et al. (2019) developed the Integrated Functional-Contextual Framework (IFCF) for understanding the role of cognitive biases in pain. This framework was inspired by the Combined Cognitive Bias Hypothesis (Hirsch et al., 2006; Everaert et al., 2012) which asserts that cognitive biases influence and interact to maintain a given disorder (e.g., social anxiety, depression etc). The IFCF posits that cognitive biases are functional phenomena influenced by changing contexts and motivational factors. More specifically, this model claims cognitive biases pertaining to pain are: i) functional, ii) dynamic and iii) inter-related and/or interacting.

Firstly, with respect to functionality, the IFCF rejects the notion that cognitive biases are inherently maladaptive, citing context as a key determinant of the adaptive value of pain. For example, if an individual was to walk to work across a very icy path, they may recognise that they are at risk of falling and potentially injuring themselves. This threat prompts the individual to alter their behaviour and walk across a less icy path where this risk of slipping is far reduced but enable the individual still to get to work in a timely manner. Here, cognitive biases are adaptive in that they promote protective responses (i.e., walking across a less dangerous path) to prevent negative pain-related outcomes (i.e., potentially falling over and injuring oneself). Hence, the adaptive utility of these biases is finely balanced between a response to prevent pain-related outcomes and the urgency/value of competing goals. However, in circumstances where protective responses are unavailable/ineffective, these biases may hinder one's pursuit of daily tasks/life goals. For example, preferentially attending to pain-

related information, interpreting ambiguous information in a threatening manner, and selectively retrieving pain-related information from memory possesses no adaptive value in chronic pain patients but instead negatively impacts their ability to complete daily tasks/life goals. Thus, it is the inflexibility/rigidity in chronic pain patient's attention, interpretation, and memory (irrespective of active goals/changing contexts) which are thought to result in negative pain outcomes.

Secondly, central to the IFCF is the notion that cognitive biases are dynamic. The IFCF rejects implicit assumptions that cognitive biases are stable trait-like processes, citing a multitude of studies that have highlighted cognitive biases are influenced by contextual and motivational factors. For instance, Notebaert et al. (2011) have shown that when avoidance of pain is a focal goal, the tendency to display attentional bias for pain-related information increases, suggesting goal pursuit as a mediating factor. On the other hand, Schrooten et al. (2012) found that attentional biases to pain were reduced when participants were presented with a salient competing goal in the form of gaining money based on task performance.

Thirdly, the IFCF holds the view that these biases are inter-related and interacting due to shared underlying mechanisms that fuel their potential co-occurrence, and that relationships between cognitive biases are bi-directional. Indeed, the framework proposes that attention is first captured by ambiguous bodily sensations, with individuals then interpreting these sensations as threatening or non-threatening. This interpretation then affects later attentional processes and how situations are potentially remembered. In instances when similar bodily sensations are experienced, the pain memory is re-activated which invariably influences attention and interpretation (see **Figure 1.2**). However, given the recency of this model, there is still a paucity of supporting (or refuting) research.

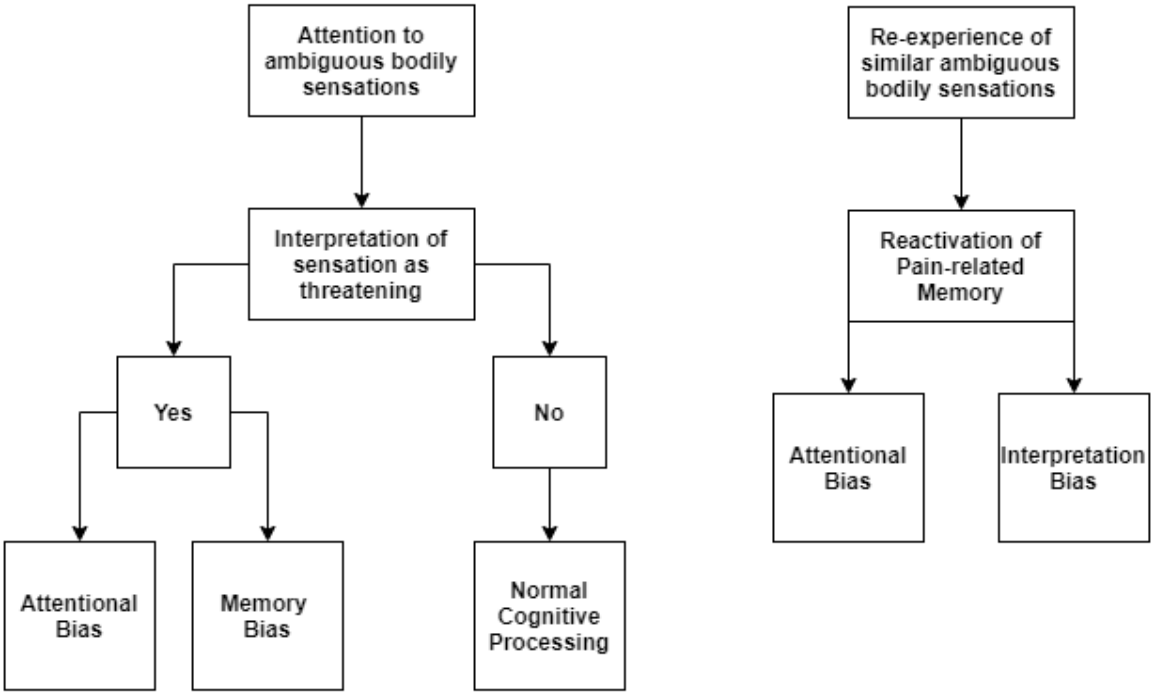


Figure 1.2: **The Integrated Functional Contextual Framework (diagram created based on written descriptions by Van Ryckeghem et al., 2018)**

1.3.8 The Utility of Cognitive-Affective Models for future Combined Cognitive Bias Research.

Cognitive-affective models have proved fruitful in attempting to allow understanding of the presence, antecedents, and consequences of cognitive biases. For example, as outlined by the FAMP, pain-related fear can fuel avoidance behaviour, which lowers the threshold at which subsequent pain is experienced (Vlaeyen & Linton, 2000). The cognitive-affective model (Eccleston & Crombez, 1999) highlights the interruptive function of pain and its relationships between pain-related characteristics (i.e., threat value) and environmental demands (i.e., emotional arousal). The SEMP (Pincus & Morley, 2001), while initially proposed as a post-hoc explanation for the observed data in their review, has since been subject to scientific investigation, with evidence indicating chronic pain patients exhibit a greater degree of enmeshment between pain and self-schema (Van Ryckeghem et al., 2013). More

recent theoretical models, including the TIM (Todd et al., 2015) and IFCF (Van Ryckeghem et al., 2019), have outlined possible relationships between cognitive biases, emphasising their interacting and interrelated nature, which has been a welcome step forward. Specifying the relationships between cognitive biases in this way enables researchers to test the key claims of these models and assess how these biases occur in a variety of functional contexts.

That said, a critique of the pain and cognitive bias literature is that studies tend to measure cognitive biases in isolation (this will be returned to in detail in section 1.3.9), hence, to be able to further evaluate the utility of these models, research measuring multiple cognitive biases within the context of a single study is vital. Indeed, such research may also indicate ways in which features of cognitive-affective models can be incorporated into a unitary framework (like that of the IFCF). For example, if pain-removal becomes a focal goal, individuals may become fixated upon seeking a biomedical solution (as outlined by the MPSM, and consistent with the Motivational Account of Attention to pain). This goal pursuit may foster a motivational context that increases the potency of cognitive biases; that is, enhanced attention towards pain, interpretation of pain as highly threatening (and thus of higher priority to resolve), and the association of contextual cues triggering memory processes associated with previous failed attempts to remove pain. It would then be plausible to suggest that individuals who are motivated to alleviate pain, despite being repeatedly unsuccessful in their attempts, may exhibit a greater degree of enmeshment of self and pain schema, due to 'ironic' rebound, whereby attempts to supress pain-related thoughts decrease the threshold at which such thoughts are experienced. In other words, the motivation to seek a biomedical solution, when not available, prevents an individual from being able to come to terms with pain, rejecting it as a part of their self-identity. Alternatively, an individual who instead of attempting to eliminate pain, is motivated to effectively manage it, may be more motivated to accept that pain is part of their self-identity, understand that their pain does not define who they are, and that they are more than their pain (i.e., they have a lower degree of enmeshment between self and pain schema). While the above is speculative, the addition of the TIM and IFCF to the field of pain enables researchers to think more creatively about how cognitive biases may operate in differing motivational contexts, and influence other important psychological constructs, such as identity.

1.3.9 Summary of Cognitive-Affective Models of Pain

While there are numerous cognitive-affective models of pain, each of which have major and minor differences, there are several factors which unite the models. For instance, all theories implicate a role of attentional bias in pain. That said, recent motivational frameworks acknowledge that situational factors determine the influence of this form of bias (e.g., Van Damme et al., 2011; Van Ryckeghem et al., 2019). Second, each model proposes associations between attention and other cognitive-affective factors (e.g., fear of pain, catastrophising, goal pursuit etc.), which drive further attentional biases. Thirdly, all models implicate a role for threat in the experience of pain, which is proposed to drive attentional biases for pain-related information and influence pain outcomes (i.e., threshold, tolerance, intensity). Fourthly, more recent models (e.g., the TIM and IFCF) have begun to outline the temporal relationship between cognitive biases, with interpretation bias preceding attentional bias (or vice-versa), and both interpretation and attention influencing subsequent memory biases. Given the above, five key hypotheses from cognitive-affective models of pain can be drawn. These are:

1) Individuals with chronic pain will display an attentional bias for pain/illness related information.
2) Individuals with chronic pain will display a tendency to interpret ambiguous information in a negative or threatening manner.
3) Individuals with chronic pain will selectively recall pain and/or illness associated information from memory.
4) Attentional and interpretation biases will be associated with poorer pain outcomes, including a reduced pain threshold, shorter pain tolerance and increased pain intensity.
5) Attentional and interpretation biases will influence the development of memory biases.

However, one key question that has yet to be considered is how these cognitive biases form – for instance, do they form prior to, or as a consequence of, an acute pain experience? Indeed, it also remains poorly understood if, and how, pain shapes cognitive biases. Hence, further laboratory work experimentally inducing pain in pain-free samples is still needed, before progressing to clinical samples, to further understand the role of cognitive biases in pain.

Thus, there is still need for pain manipulation in non-chronic pain samples. This question will be returned to, and is the focus of, Chapter 5.

1.4 Pain-related Cognitive Biases in Adults

In recent years, significant research efforts have been dedicated towards investigating the role of cognitive biases in the aetiology and maintenance of chronic pain. The term 'cognitive biases' is frequently used to encompass three key biases that result in the preferential processing of information concordant with one's own motivations, interests, and concerns. To expand, there are three main forms of cognitive bias, these include the preferential allocation of attentional resources to threatening stimuli relative to neutral stimuli in one's environment (this is ***attentional bias***), the interpretation of ambiguous information in a negative or threatening manner (this is ***interpretation bias***), and the ability to retrieve negative/threatening information from memory (this is ***memory bias***).

Although the nature of these biases is different, there is evidence to suggest that each plays a role in the development and maintenance of many psychiatric disorders. For instance, individual's suffering from anxiety, depression and anorexia nervosa display attentional bias to anxiety, depression, and food congruent material respectively (Bar-Haim et al., 2007; Peckham et al., 2010; Brooks et al., 2011). Patients with social anxiety and depression have been found to interpret ambiguous information in a negative way, thus displaying interpretation bias (Amir et al., 2005; Mogg, et al., 2006). Moreover, clinically, and sub-clinically depressed individuals have been shown to recall more unpleasant information from memory, thus displaying memory bias (De Raedt & Koster, 2010). With regards to patients suffering from chronic pain, it is widely acknowledged that these cognitive biases operate in a similar fashion but exert their influence through the preferential processing of information that depicts the importance of bodily threat and harm (Lau et al., 2019). Considering this, a fuller overview of current knowledge as to the role these biases play in pain is presented below.

1.4.1 Attentional Bias – findings, limitations, and future directions.

Selective attention towards threatening stimuli over neutral stimuli in one's environment is highly adaptive (see Maratos and Pessoa, 2019), resulting in faster detection of threat (Liossi et al., 2014), greater difficulty disengaging from threat (Brookes et al., 2017) and/or avoidance of threat (Van Damme et al., 2004). Pain is argued to interrupt, distract and demand attention (Eccleston & Crombez, 1999). These characteristics may be adaptive in an acute pain environment, for instance, attending to the feeling of pain when moving an injured limb, and subsequently avoiding the use of that limb to promote healing. However, in a chronic pain environment, where the source of pain cannot be removed and individuals cannot escape or avoid the pain, several pathological responses can occur. To expand, chronic pain can cause an individual to preferentially attend to pain-relevant information. The continuous effort to detect painful sensations and other pain-related information can fuel hypervigilance to pain, which can lead to a wide variety of pathological responses, including the development of depression and anxiety (Fishbain et al., 1997; Campo et al., 2004; Woo et al., 2010), avoidance of physical activity/movement (Vlaeyen & Linton, 2000; Leeuw et al., 2007), and isolating oneself from friends and/or family (Asmundson et al., 2004; Crombez et al., 2005). Indeed, more recent research has reported that avoidance of pain-related stimuli (i.e., affective pain words) during the acute pain stage can increase the likelihood of the development of chronic pain (Sharpe et al., 2014). As such the role of attentional bias (AB) in the modulation of pain has received significant research interest over the past decade, although the evidence for AB among chronic pain populations has been mixed.

In overview, using a range of experimental paradigms (which are reviewed in Chapter 2), attentional bias has been demonstrated in several chronic pain conditions, including musculoskeletal pain (Schoth et al., 2015), rheumatoid arthritis (Sharpe et al., 2009) and chronic headache (Liossi et al., 2011). Yet, other studies, using the same populations, have reported no such biases (Roelofs et al., 2003; Asmundson & Hadjistavropoulos, 2007), indicating the field is marked by large variability in findings. Indeed, Schoth and Liossi (2012) conducted a meta-analysis of ten visual-probe investigations and found evidence to suggest that chronic pain patients show significantly greater attentional biases towards pain-related stimuli than control participants. Additionally, they found that the time-course of attentional bias with chronic pain patients reflected greater attentional bias during the later stages of

attentional processing (i.e., *maintained attention*), as opposed to the earlier stages of attentional processing. That said, a more recent meta-analysis of studies investigating attentional bias in a number of different pain populations by Crombez et al. (2013) observed mixed findings. While there was evidence to suggest that patients with chronic pain did display an attentional bias towards pain-related words and images, this bias was of a small effect size and did not differ from controls. What is more, no evidence was found for attentional bias towards pain-related words or pictures for acute, procedural, and experimental pain. Hence, the evidence for AB in pain research is often contradictory, equivocal and/or difficult to disentangle.

To explain the mixed findings in AB research, Dear et al. (2011) examined whether two stimulus-related factors; i) the personal relevance of stimuli and ii) their ecological validity, influence the detection of pain-related attentional biases. To achieve their aims, two visual-probe tasks were developed, a word-based visual-probe task (i.e., lower ecological validity) and a picture-based visual probe task (i.e., higher ecological validity) to detect attentional biases using generally selected (i.e., lower personal relevance) and idiosyncratically selected stimuli (i.e., higher personal relevance). Attentional biases were found among chronic pain patients and pain-free controls for idiosyncratically selected pictorial stimuli presented using a picture-based visual probe task (highest ecological validity and personal relevance), but not for generally selected pictorial stimuli or for idiosyncratically/generally selected pain-related word stimuli. Thus, Dear et al. (2011) concluded that stimulus-related factors may be important to the detection of attentional biases in pain-related research.

Of note, there has been considerable debate surrounding the use of pain-related word and pictorial stimuli to measure AB in patients with chronic pain. For instance, some researchers have questioned the ecological validity of word stimuli, as word stimuli involve cognitive processing and are hence limited in early-stage threat value (Dear et al., 2011; Bar-Haim et al., 2007). Pain-related pictorial stimuli, coversely, are not only more ecologically valid but have been used in a number of domains, particularly research focusing on cognitive biases and emotion processing (Palomba et al., 1997; Bradley et al., 1999; Giel et al., 2011).

Regardless of the stimuli selected to measure AB, a critique of many studies is the failure to consider the emotional properties of their stimuli. For example, valence (the pleasantness or unpleasantness of a stimulus) and arousal (how strongly the stimulus makes us feel) have been shown as important emotional components that capture attentional resources

(Lang, 1993). That said, there are a number of broad-topic databases that contain measurements of valence and arousal for their pain stimuli, including the International Affective Picture System (IAPS, Lang et al., 1997; Lang & Bradley, 2007), Geneva Affective Picture Database (GAPED, Dan-Glauser & Scherer, 2011), and the Psychology Image Collection at Stirling (PICS, pics.stir.ac.uk). However, it can be argued that other emotional properties are of equal importance in pain-related research – for example, threat value (the degree to which a stimulus is percieved to be threatening) and pain intensity (the perceived intensity of the pain in the stimulus). Given that theoretical models (TIM, Todd et al., 2015) implicate emotional properties, for example, threat value as a factor that can determine whether an individual displays normal attentional processing or a vigilance-avoidance pattern of processing, it is clear that studies should assess the emotional properties of their stimuli prior to data collection given their theoretical significance.

Careful consideration is also needed when selecting the experimental paradigm to detect attentional biases. Researchers have questioned the ecological validity of indirect (i.e., response time oriented) measures of attention (which are described and evaluated in Chapter 2), because they cannot fully capture the dynamic nature of attention (Waechter et al., 2014). Additionally, reaction time, assumes that gaze location corresponds to motor (usually manual) responses, which is not always the case (Fashler & Katz, 2014, 2016). Hence, eye-tracking technology is the gold-standard for measuring attentional biases related to chronic pain, given that it provides a direct measure of overt attentional deployment. To date, research has shown that individuals with CP have faster first fixation latencies for pain-related stimuli than HCs, providing evidence of vigilance during early attentional processing, while other studies have reported the exact opposite, with enhanced vigilance during later attentional processing (see Priebe et al., 2021). Hence, clear evidence for a vigilance-avoidance AB as predicted by the TIM (Todd et al., 2015) has yet to be provided. Albeit this pattern of processing has been observed in a pain-free sample (see Priebe et al., 2015). Chan et al., (2020) conducted a systematic review and meta-analysis of the pain-related, eye-tracking literature. Results revealed no significant differences between chronic pain patients and healthy controls in terms of their eye-movements on pain-related stimuli. That said, preliminary evidence was found for gaze biases varying across chronic pain sub-types. In an attempt to explain these findings, the authors cited the methodological heterogeneity of the literature and the small number of studies available for direct comparison. Most recently, Blaisdale-Jones et al., (2021) examined the time

course of AB in studies employing eye-tracking technology with CP patients of any age and HCs. No between-groups differences were observed, however, within-groups differences revealed a significant AB towards pain-related words and/or pictures on probability of first fixation, the amount of time spent looking at the pain words and/or pictures below 500ms, and the total amount of time spent focusing on pain words and/or pictures. Consquently, the authors concluded that while evidence was found to support biases in vigilance and attentional maintenance for pain related stimuli, ABs are ubiquitous and not influenced by pain status. Considering the above, in order to gain a more detailed insight as to whether individuals with chronic pain display an AB for pain-related information the use of eye-tracking technology and homogenous task designs would help to disentangle the presently mixed literature. Indeed, not only would this allow researchers to answer more broader questions, but equally investigate more complex ones, such as the time course of ABs to pain-related stimuli.

1.4.2 Interpretation Biases – theoretical relevance, limitations, and implications.

The tendency to interpret innocuous situations, symptoms or sensations in a negative or threatening way has been studied in a number of clinical populations, including patients suffering from anorexia and bulimia (Cooper, 2005; Williamson et al., 2000), depression (Mogg et al., 2006; Everaert et al., 2013) and chronic pain (for review see Pincus & Morley, 2001). Similar to that of AB, interpretation biases (IB) are believed to act as vulnerability factors that can aid the development and exacerbation of pain problems in those who are susceptible to developing chronic pain (Vancleef et al., 2009). Indeed, numerous theoretical models including the FAMP (Vlaeyen et al., 2016), TIM (Todd et al., 2015), MDPSM (Eccleston & Crombez, 2007) and IFCF (Van Ryckeghem et al., 2019) specifically implicate IB in the development/maintenance of chronic pain symptoms. For example, the interpretation of pain as threatening/harmful is thought to encourage pain patients to avoid normal activites that promote recovery, contributing to a vicious cycle that develops/maintains pain. Similarly, the degree to which pain is interpreted as threatening is also proposed to influence other cognitive biases, specifically, the attentional processes exhibited (i.e., hypervigliance or avoidance) and the pain-related information selectively recalled and/or recognised. Researchers have also generated speculative hypotheses regarding the role of avoidance in IB research. Khatibi et al., (2015) proposes that as one's pain level increases, so too does their level of threat and, under circumstances of very high pain and threat, avoidance may ensue promoting the suppression of IBs. Thus, gaining a more detailed understanding of the role of IB and it's interaction with AB and MB is of both theoretical and clinical importance.

Generally speaking, the pain literature distinguishes between two different forms of IB. These include explicit and implicit IB. Explicit IB refers to the conscious cognitive processing of ambigiuous stimuli, with biased judgements clearly distinguishable from unbiased judgements (e.g. pain/illness interpretations vs neutral/benign interpretations). Conversely, implicit IB refers to the relatively unconscious and automatic processing of stimuli, and unlike explicit interpretation bias, cannot be inferred directly from a persons' behaviour or responses. Instead, implicit IBs are inferred from interpretations made immediately when confronted with ambiguity. As such, a

number of different experimental paradigms are used to measure explicit and implicit IBs (discussed in detail in Chapter 2). Direct measures of interpretation bias are used to measure explicit IBs (e.g., homophone/homograph tasks, word-stem/sentence-completion tasks etc). In contrast, indirect measures of IB (e.g. the online interpretation paradigm and the incidental learning paradigm) are used to measure implicit IBs (Vancleef et al., 2009; Khatibi et al., 2015).

Unlike the AB literature, early research investigating IBs in pain has repeatedly found evidence for a negative IB amongst chronic pain populations. For example, Pincus et al., (1994) found that when presented with ambiguous cues in the form of homographs (e.g., terminal, wrenching, growth), patients with chronic pain produced more pain-related associations (e.g. illness, pain, cancer) than an osteopathic and control group. Similarly, McKellar et al. (2003) found that when presented with a homographic response task, participants in the chronic pain group were significantly more likely to respond to homographic stimuli in a pain-related manner than two comparision groups comprising of acute pain patients and medical staff respectively. Evidence for IBs in chronic pain populations also comes from a recent systematic review and meta-analysis conducted by Schoth and Liossi (2016). Seven studies comprising chronic pain patients (n = 445), pain-free controls (n = 407) and healthcare professionals (n = 170) using four different experimental paradigms (word stem, homographic response, homophone task, incidential learning task) were identified and included. All 7 studies provided evidence to support the notion that chronic pain patients, relative to healthy controls, interpret ambiguous words and images in a pain/illness-related manner. Indeed, meta-analytic data for 4 of the studies revealed a large effect size (.67). Consequently, the authors concluded that there is clear evidence that participants with chronic pain display a tendency to interpret amibguous information in a pain and/or illness-related manner (Schoth & Liossi, 2016).

Despite the significant findings outlined above the paradigms commonly used to measure IB have come under considerable scruitiny in recent years. For instance, direct measures of IB such as the homographic response task have been criticised on the grounds that threatening and neutral associations often have different written and verbal frequencies of use (Schoth & Liossi, 2017). For instance, ‘pain’ has more strong associations than ‘pane’ and is therefore unlikely to be

suitable for use as an ambiguous homophone. Upon hearing this homophone, participants are likely to interpret this as 'pain' irrespective of whether they suffer from chronic pain or not, thus reducing the likelihood of observing between-group differences. Additionally, indirect measures of IB have been criticised for the use of morphed facial expressions which appear unnatural, thus lacking ecological validity; and for also inferring IB from response times.

In an attempt to address the aformentioned limitations new measures of explicit IB have been developed. For instance, Heathcote et al. (2016) developed the Adolescent Interpretations of Bodily Threat Task (AIBT, full description provided in Chapter 2). The AIBT involves presenting participants with ambiguous scenarios. For example, *"Someone kicks a ball and it hits you in the face. In the mirror you see your face is covered in…".* Participants are instructed to read and imagine themselves in the situation and then select one of two researcher-generated end words that resolves the situation in a pain-related manner (i.e., blood) or benign manner (i.e., mud).

Heathcote et al. used the AIBT to measure explicit IBs in a sample of healthy adolescents (study 1) and adolescents with chronic pain (study 2). In the first study, healthy adolescents who catastrophised about pain and those who reported more recent pain issues were found to endorse more negative and reject more benign interpretations of ambigiuous scenarios with a medium to large effect (Heathcote et al., 2016). In the second study, the AIBT task was presented to two groups of adolescents; one with chronic pain and one without. Results showed that adolescents with chronic pain were less likely to endorse benign interpretations of ambiguous pain and bodily threat information than their healthy adolescent counterparts, particularly when reporting on the strength of the belief in those interpretations being true (Heathcote et al., 2017). Indeed, when severity of chronic pain and pain catastrophising were controlled for, this interpretation pattern was still found to be associated with increased disability among adolescent patients. Relatedly, Lau et al (2019) investigated the context-specificity of pain-related interpretation biases in adolescents using an adapted version of the AIBT task developed by Heathcote et al. (2016). Findings showed that adolescents with low and moderate-to-high pain interference endorsed more negative interpretations across all situations and were less likely to display a benign interpretation style compared to adolescents without interfering pain.

However, a key limitation of the AIBT is that participants are constrained by a forced-choice response format, with only one of two possible interpretations available to be selected. Thus, it is questionable as to whether the end word selected accurately reflects the participant's own interpretation of each scenario. Indeed, the AIBT has only been used in an adolescent population posing age constraints. Therefore, there is a need for future research to develop paradigms with a free-choice response format to provide a more accurate measure of IB. Not only would this help to advance pain theory with respect to greater insight into the role of IB, but this may also present implications for intervention. For example, Cognitive Bias Modifications for Intervention (CBM-I) have started to develop in other areas of Psychopathology, namely, anxiety and depression (for review see Cristea et al., 2015). Hence, the development of ecologically valid measures of pain related IB may help to contribute to/assess interventions that seek to promote a more positive interpretation style, reducing the tendency to interpret ambiguous situations as painful and consequently break the vicious cycle of chronicity, which IB is thought to be a maintaining factor of.

Taken together, research suggests that adults and youth with (chronic) pain display a negative IB in favour of pain/illness-related interpretations. However, the paradigms employed in these studies have been criticised for possessing a lack of appropriate stimuli, low ecological validity and constraining participants to forced-choice response formats. Therefore, future research/paradigm development is necessary to gain a more detailed insight as to the role of IB in pain, potentially contributing to the advancement of pain theory and interventions designed to modify IB.

1.4.3 Memory Bias – recall, recognition, or both?

Over the past two decades research has investigated other cognitive factors that may contribute to the aetiology and maintenance of chronic pain., including memory bias (Mezza et al., 2018). To recap, memory bias is defined as the tendency to selectively retrieve and/or recall pain and illness associated information from memory. There is evidence to support the notion that individuals who

repeatedly experience pain display biases in memory for pain associated stimuli, including enhanced recall of said stimuli compared to their non-pain counterparts (for review see Pincus & Morely, 2001). The prevailing theoretical account of these findings is Bower's (1981) Associative Network Theory. According to this theory, emotions are represented in 'nodes' which are defined as cognitive representations of clusters of memories associated with a particular emotion (e.g., anger, happiness, depression etc.). For instance, when applied to depression, this theory asserts that when an individual feels depressed, a corresponding 'depression node' activates. This reduces the threshold for processing depression congruent material, subsequently facilitating encoding and retrieval processes. Applied to the field of chronic pain, this theory assumes that there is a specific node that represents pain, which is associated with other nodes containing different memories for pain-related experiences. Individuals who recurrently experience pain may therefore develop a bias in memory for pain-related stimuli due to the reduced threshold for processing pain-congruent material and the repeated activation of these nodes causing pain-related memories to regularly enter consciousness. Thus, like mood, pain is proposed to bias mnemonic processing.

As with IB, there are two types of memory bias: implicit (non-declarative) and explicit (declarative, Eysenck & Byrne, 1994). Implicit memory bias refers to the ability to inherently recall past events and information without requiring conscious effort to remember them. Explicit memory bias involves the conscious and intentional recollection of information (e.g., factual, previous experiences etc.). When information has been stored in memory it can be retrieved directly in the case of explicit memory or indirectly in the case of implicit memory. The most robust measure of explicit memory bias is recall bias. In pain research, this typically involves presentation of a list of words (containing pain-related and neutral words). A distractor task is then used to clear any words in short-term memory and prevent new information transfering to long term memory. Participants are then asked to recall as many words as possible from the previously presented word list within a given time frame. It is important to note, however, that retrieval instructions vary considerably among studies. For instance, in recent years studies have used indirect measures in which participants are not explicitly asked to remember the stimuli presented, such as word completion tasks (Schoth et al., 2018).

As alluded to previously, there is support for the notion that patients with chronic pain display recall bias towards pain-related stimuli (Pearce et al., 1990; Edwards et al., 1992; Edwards & Pearce, 1994). Early research by Pearce et al. (1990a) examined memory function in chronic pain patients using free recall methodology. It was found that at delayed recall (of 5 minutes in duration) chronic pain patients recalled significantly more pain words than neutral words and more negative words than positive ones. Additionally, following the 5 minute interference task, whilst participants with chronic pain recalled fewer words overall, they still recalled more pain words than neutral words and more pain words than negative words. Interestingly, the word 'pain' was found to be significantly more likely to be reported by pain patients with 18% recalling this word immediately and 15% after 5 minutes, while control participants did not report this word on either occasion. Hence, the findings of this study clearly illustrate that patients with chronic pain display a recall bias towards pain-related stimuli. Further research conducted by Edwards et al. (1992) recruited four groups comprising of depressed and non-depressed chronic pain patients, depressed psychiatric patients and non-patient controls. Prior to a free recall task, participants were presented with a series of pain-related (sensory, affective) and neutral adjectives. The results showed that the non-depressed chronic pain patients exhibited a significant recall bias for the sensory pain adjectives. Furthermore, while their depressed chronic pain counterparts displayed high recall for both sensory and affective pain adjectives, this finding did not reach statistical significance. Hence, the findings indicate that recall bias is influenced by factors other than the elevated depression levels commonly reported in chronic pain patients (Rayner et al., 2016). Edwards et al. (1992) concluded that both chronic pain groups demonstrated specific recall biases directly related to pain and depression compared to controls, indicating that the sensory and affective components of the experience of pain have distinct effects on memory. Subsequent research by Edwards and Pearce (1994) tested implicit memory in chronic pain patients using unprimed words (i.e., words which have not been seen prior to 'recall'). Each group was required to complete 12-word stems using the first two English words that came to mind. In a word stem task the participant is presented with the first 3 letters of a word (e.g., *Hor_ _ _ _)* and is required to complete the rest of the word stem as quickly as possible. Word stems are ambiguous in that they can be interpreted in a neutral (Hor*izons*) or threatening manner (*Horrible).* Importantly, Edwards and Pearce (1994) used word

stems that could be completed in a pain-related (e.g., sensory, affective, illness) or neutral (e.g., non-pain) manner. Results showed that the chronic pain group produced significantly more pain-related completions than did the health professional and control groups. This indicates that the personal experience of pain is an important factor in the development of altered patterns of information processing.

Although studies have found evidence to suggest that patients with chronic pain display recall biases, it must be noted that there are conflicting findings in this area. Busch et al. (2006) recruited patients suffering from chronic neck pain and healthy contols, and presented them with two novel computerised pictorial memory games (one pain, one neutral) and two free-recall tasks. Results showed that participants with chronic neck pain performed significantly worse than their non-pain counterparts in the pain memory game. What is more, no significant differences in performance between both groups for the neutral memory game and the two free-recall tasks were observed, thus contradicting previous research in this area. In an attempt to explain their findings Busch et al. (2006) speculated that the chronic pain group may have used cognitive avoidance in an attempt to ignore and/or distract themselves from the pain-related stimuli. More recently, Karimi et al. (2016) investigated recall bias in patients with CLBP and healthy controls. No evidence of recall bias in terms of the number of pain words correctly recalled was found. That said, when CLBP patients were classified into patients with a fear-avoidance response (FAR), endurance response (ER) or adaptive response (AR) important differences in the processing of pain words emerged. To expand, patients with FAR recalled less pain-related words than neutral words in a free recall task, indicating avoidance of pain-related information. On the other hand, patients with ER were found to recall more pain-related words than neutral words.

In addition to recognising patients' response patterns, research suggests that the differentiation of depressed and non-depressed chronic pain patients is also important. Pincus et al. (1995) recruited a sample of depressed and non-depressed chronic pain patients and found that depressed pain patients showed enhanced processing of pain-related stimuli, but not for depression-related stimuli. Additionally, non-depressed pain patients were found to not exhibit a recall bias for negative pain-related information. To explain the observed findings pertaining to

depressed chronic pain patients, Pincus et al. (1995) speculated that patients who experience pain for a long duration develop a processing bias towards sensory-pain information (somewhat consistent with the IFCF). However, for some pain patients this may also include a processing bias for pain-distress information, a negative self-image, and higher levels of depression. Hence, given that depressed pain patients endorse and recall negative self-referent pain adjectives, but do not show a bias towards self-referent depression content, this indicates that the depression associated with chronic pain is different from the depression experienced by patients without pain. More specifically, that pain-related distress is distinguishable from clinical distress, emphasising a strong connection between mood states, pain, and cognitive processing.

Most recently, Schoth et al. (2020) provided a contemporary systematic review and meta-analysis of studies investigating memory bias in adults with chronic pain. Of the 18 studies elegible for inclusion, subset meta-analyses were reported for 12 studies that enabled comparison between chronic pain patients and healthy controls. It was found that relative to healthy controls, chronic pain patients showed a significantly weaker recall bias for affective-pain words. However, this only occurred when non-depressed chronic pain patients were included. No significant differences emerged between chronic pain patients and healthy controls in relation to the recall of sensory-pain, illness-related or depression-related words. That said, within-groups analysis revealed that chronic pain patients displayed a significant recall bias favouring sensory pain words relative to neutral or affective pain words, and a significant recall bias for illness-related words relative to depression-related words. Taken together, the authors concluded that while there is evidence of an enhanced recall bias favouring sensory-pain words relative to neutral words in adults with chronic pain (supporting the IFCF), the overall evidence for pain-related memory biases in adults with chronic pain is inconclusive. Schoth et al. (2020) highlighted a number of methodological limitations which may have contributed to their findings. Namely, i) few studies obtained measures of valence and arousal for their stimuli, ii) many failed to report using an appropriate testing environment for all participants, and/or iii) did not match chronic pain patients and healthy controls according to demographic variables including age, sex and educational level. Considering the above, it is clear that there is much yet to be discovered with respect to the role MB plays in the development and maintenance of chronic pain.

The extent to which individuals with pain display a recognition memory bias favouring pain-related information, nontheless, has received little empricial investigation to date. This is surprising as recognition paradigms (as compared to recall paradigms) have been argued to be a more ecologically valid measure of MB given more efficient retrieval cues and the involvement of comparison processes between the available and stored information (Maratos et al., 2020). Interestingly, previous research utilising recognition paradigms has revealed important findings. Wimmer and Buechel (2016) examined whether thermal heat pain influences long-term memory for single events (episodic memory) using *fMRI*. In this study, participants experienced heat pain varying in intensity (high, low) whilst being presented with neutral pictures (i.e., household objects). Participants then completed an immediate (surprise) memory test to assess recognition strength and memory pertaining to the level of pain concurrently administered with the object. One year later, participants also completed a surprise recognition test. Findings revealed that in the immediate memory test there was no effect of pain on episodic memory strength. However, in the recognition task presented one-year later, pain was found to enhance memory with higher accuracy rates observed for images paired with heat pain (low, high). The authors concluded that pain modulates memory for neutral stimuli. Similar findings have also been observed by Schwarze et al. (2012) who found that painful electric shocks had no effects on immediate recognition in an image-categorisation paradigm, thus initially suggesting pain does not influence memory. However, when replicating this study but testing participants a day later, memory performance was found to be enhanced for pain-paired items (Schwarze et al., 2012). Taken together, these findings highlight enhanced recognition following an acute pain experience which appears to emerge after a period of consolidation. Indeed, the findings of Schwarze et al. (2012) are perhaps unsurprising, given that pain stimuli attract attention during initial encoding, and therefore are more likely to be subsequently remembered.

However, much like the recall bias literature, the findings pertaining to recognition bias are also mixed with studies reporting findings contradictory to those outlined above (Flor et al., 1997; Kuhajda et al., 2002; Grisart et al., 2007; Forkmann et al., 2016). Grisart et al. (2007) investigated the impact of chronic pain on memory functioning in a recognition task. Using a Remember/Know (R/K) procedure, chronic pain patients were found to show a decrease in the recollection of neutral

words (R responses) and an increase in feelings of familiarity for these words (K responses), compared to their non-pain counterparts. That said, the above pattern of performance was not found to be related to overall recognition ability. Participants with pain (e.g., headache) have also been shown to recognise fewer words than participants without pain during a recognition task (Flor et al., 1997; Kuhajda et al., 2002). Albeit it should be noted that in the study by Kuhajda et al., (2002) the presence of headache (or no headache) did not have a significant impact on memory. This is consistent with previous research by Forkmann et al. (2016) who recruited a sample of healthy participants and presented them with an encoding task which involved the presentation of neutral images (comprising living/non-living objects) concomitantly with or without heat pain stimuli. Following this, a surprise recognition task was then immediately presented, comprising all the images presented previously in the encoding task (old stimuli) mixed with a matched number of previously unpresented images (new stimuli). Participants were asked to indicate whether they had been presented with heat pain, or no heat pain when the image had been previously displayed. Results revealed that experimentally inducing pain via heat stimulation impaired recognition accuracy (both recollection and familiarity), with recognition memory being lower for images presented with painful heat – indicating that pain interfered with the visual encoding of the images. Hence, there is some evidence for the negative impact of pain on recognition in both clinical and experimental pain samples.

To conclude, the evidence for pain-related recall bias is presently inconclusive and mixed. There is preliminary evidence to suggest that individuals with pain display recognition biases, but the exact nature of these biases is unclear. Therefore, more research is needed to examine these biases, and if found, the role they play in pain. Further questions remain - for example, if individuals do display memory bias for pain-related stimuli how does this change over time? Additional research may also help to test key theoretical assumptions – to expand, Bowers' (1981) Associative Network Theory would predict chronic pain patients to have a reduced threshold for processing pain-congruent material due to repeated activation of a pain node, consequently, pain-related memories should enter consciousness more regularly causing a pain memory bias. Hence further research is needed as the nature of pain-related memory biases in adults with pain is inconclusive.

1.4.4 Attention, Interpretation and Memory biases – summary, limitations and future directions.

To summarise, the AB literature has been plagued by issues surrounding hetereogeneity in paradigm use which has often resulted in mixed and contradictory findings contributing to a literature base that is difficult to disentangle. Additionally, given that pain-related word stimuli lack ecological validity, the incorporation of pain-related pictorial stimuli would be appropriate for future studies. However, consideration of the emotional properties (valence, arousal, pain intensity, threat value) of said stimuli is important given that they are implicated in theoretical predictions. To recap, the TIM (Todd et al., 2015) proposes that low threat results in normal attentional processing, whereas high threat results in the display of a vigilance-avoidance pattern of processing. Therefore, validating pain-related images from broad-topic databases to gain measurements of their emotional properies would increase ecological validity and enable a more accurate and reliable investigation of pain-related AB.

With respect to IB, evidence is generally consistent in the reporting of a negative interpretation bias for pain-related information in adults with chronic pain (see Schoth & Liossi, 2016). However, similar to the AB literature, there are methodological limitations of the paradigms used. These include a lack of appropriate stimuli due to issues associated with written/verbal frequencies (specific to Homophonic/Homographic Response Tasks) and the use of unecological stimuli including morphed facial expressions, which do not reflect facial expressions encountered in real life. Indeed, whilst progress has been made with respect to the development of novel paradigms such as the AIBT (Heathcote et al., 2015) to measure IB using ambiguous scenarios, key issues remain such as the use of a forced-choice response format. Forced-choice response formats constrain participants to pre-determined interpretations which may not accurately reflect the participants' own interpretation of the scenario. That said, while evidence of a negative interpretation bias in youth has been found using the AIBT (Heathcote et al., 2015, 2016, Lau et al., 2019), ambiguous scenarios have yet to been validated for use with adult populations. Hence, developing an AIBT task using free and forced-choice response formats suitable for use with adults would enable proper and rigourous investigation of IB .

Lastly, despite some studies reporting evidence for enhanced recall of pain-related information, a recent systematic review by Schoth et al., (2020) concluded that the current state of evidence is 'inconclusive'. In their review, Schoth et al., highlighted methodological limitations of previous research, including overlooking the importance of emotional properties, hetereogeneity in task instructions and the use of inappropriate testing environments. Moreover, the above review focused solely on studies examining biases in recall, despite some evidence for the enhanced recognition of pain-related information (Pincus et al., 1995) demonstrating a dearth of recent research into recognition biases and their role in memory. Lastly, to date, little research, if any has examined if (and how) pain-related MB change over time; that is, there are no studies examining immediate memory biases for pain and how those biases change over a period of weeks. Consequently, further research is needed to examine both recall and recogniton biases in the context of pain and if over a longer retention period changes in MB occur.

1.4.5 Why study Combined Cognitive Biases?

Individuals with chronic pain have been shown to display attentional, interpretation and less consistently memory biases for pain-related stimuli, as summarised above. However, a key limitation of current research is that these cognitive biases have typically been studied in isolation. While this approach helps to further our understanding of each individual bias, it fails to provide insight as to how these biases interact with one another to influence the development and maintenance of chronic pain. To develop effective pain management interventions, we need to understand whether these biases exist, and, potentially, interact or influence each other.

It is important to recognise that in recent years a number of theoretical models have been proposed to explain the role of cognitive biases in pain. To recap, the TIM (Todd et al., 2015; section 1.2.3.5), posits that interpretation bias precedes attentional bias, and that in order to respond to pain-related stimuli (e.g., words), participants must first interpret these stimuli as pain-related. When confronted with ambiguity (e.g., words such as 'sharp' or 'boring') it is argued that interpretation biases which favour pain-related interpretations are necessary for an attentional bias

to be observed. Once a stimulus has been interpreted as pain-related, the TIM speculates that the degree to which an individual shows an attentional bias towards the stimulus is dependent on its salience (i.e., how threatening one perceives it to be; low, medium or high). This model predicts that low threat should lead to easy disengagement of attention; moderate threat to more difficulty disengaging attention; and high threat to attentional avoidance.

Conversely, in the wider anxiety and depression literature attentional bias is argued to precede interpretation bias. For example, cognitive models (for review see Everaert et al., 2013) suggests that in depressed samples, once negative information enters participants' focus of attention they exhibit difficulties in disengagement, resulting in extensive elaboration and biased interpretation. The attributed meaning is then stored in their long-term memory contributing to memory biases (Everaert et al., 2013). Hence, AB indirectly impacts MB through IB. These assumptions appear to share some similarity with the Integrated Functional-Contextual Framework (IFCF) by Van Ryckeghem et al. (2019). To recap, this framework proposes that early attention is captured by ambigious bodily sensations, which are then interpreted as either threatening or non-threatening. This then impacts later attentional processes and how situations are potentially remembered contributing to a memory bias. When similar body sensations are experienced in the future, this pain memory may become re-activated affecting attentional and interpretation biases.

At present, only five groups of researchers have attempted to measure mutliple cognitive biases in a single study. Initial research by Todd et al. (2016) sought to investigate whether attention and interpretation biases are influenced by percieved threat and their interrelationship, and whether these biases predict pain outcomes (i.e., pain tolerance, threshold and intensity) in a sample of healthy university students. It was found that participants who received reassuring information regarding an imminent painful procedure (i.e., cold-pressor task) showed an attentional bias towards happy faces in a dot-probe task. Furthermore, avoidance of affective pain words was found to be associated with increased pain. That said, no relationship was observed between attention and interpretation biases, and intepretation biases were not found to be influenced by threat or associated with pain. Consequently, the authors concluded that while the findings lend partial support to the TIM (i.e., attentional bias towards happy faces can be

considered as avoidance of pain faces), to observe relationships between cognitive processing biases, a clinical sample may be needed.

Research by Hughes et al. (2017) addressed the lack of research with a clinical sample by investigating whether participants with Chronic Fatigue Syndrome (CFS) display: i) an attentional bias for CFS-related stimuli; and ii) show a tendency to interpret ambigious information in a somatic (i.e., illness-related) way. Results showed that compared to controls, CFS participants were significantly more likely to display an attentional bias for CFS-related stimuli and a tendency to interpet ambigious information in a somatic way, when controlling for depresison and anxiety. Further, these attention and interpretation biases were found to be associated with fear-avoidance beliefs and somatic interpretations were also associated with all or nothing behaviour and catastrophising. Hence, this study provides clear evidence to suggest that patients with CFS demonstrate illness-specific biases in information processing (i.e., AB and IB) that may play a role in maintaining symptoms by reinforcing unhelpful illness beliefs and behaviours.

More recently, two studies conducted by Schoth et al. (2018, 2019) revealed a number of important findings in relation to combined cognitive biases and pain. The aim of their first study was to provide a preliminary investigation of combined cognitive biases for headache specific sensory-pain words and general disability words in patients suffering from Chronic Headache (CH). They found that these patients showed a significantly greater interpretation bias for both headache specific sensory-pain words and general disability words and, memory bias, via enhanced recall for the headache specific sensory-pain words. However, no evidence of an attentional bias was observed. The results of this preliminary investigation provide evidence for interpretation and memory biases in individuals with CH. In a later study, Schoth et al. (2019) aimed to explore attentional, interpretation and memory biases and their interrelationships in patients suffering from CH. Unlike their previous investigation, results revealed that CH patients displayed significantly greater attention and interpretation biases. That is, CH participants showed preferential processing of sensory pain words compared to healthy controls during the earlier stages of attentional processing (i.e., circa 500ms), and produced more pain responses to sensory pain words. However, no biases in memory were observed, with participants in the CH group

showing no differences in the number of solutions recalled compared to their non-CH counterparts. Further, no correlations were found between attention, interpretation and memory biases. That said, it is important to note that this study used unecological stimuli (i.e., words) which require more cognitive processing during early attention and lack initial threat value. Additionally, Schoth et al., measured AB prior to IB. Given that the TIM argues that interpretation bias precedes attentional bias, and that the threat value of the stimuli is important in influencing the cognitive processes observed, this may provide an explanation for the non-significant results observed. For example, it could be that the word stimuli used were interpreted by participants in the CH group as non-threatening (as compared to non-painful), subsequently displaying normal attentional processing as predicted by the TIM. In any case, the authors concluded that their study is one of very few to measure multiple biases, thus further research is needed to test the temporal relationship between AB and IB.

Chan et al., (2020) investigated attention and interpretation biases in a sample of participants with and without chronic pain. IB was assessed via an Interpretation Bias Task which presented ambiguous scenarios that could be interpreted in a pain-related or benign manner. AB was assessed via a novel eye-tracking task that presented neutral faces with ambiguous pain/health-related labels (e.g., doctor, patient, healthy people). Adults with chronic pain were found to endorse more negative interpretations for ambigous scenarios relating to immediate bodily injury and long-term illness relative to their healthy conterparts. However, no between-groups differences for the neutral (but differently labelled) faces was observed in terms of eye-movements. That said, within-groups differences were observed with those who interpreted the illness-related scenarios in a negative manner, focusing more on the nose region and less on the eye region of the ambiguous faces with ‘patient’ and ‘healthy people’ descriptors. Hence the findings of this study provide evidence of interplay between multiple forms of cognitive biases, supporting the notion that AB and IB interact and influence one-another as proposed by the Integrated Functional Contextual Framework (Van Ryckeghem et al., 2019). However, notable limitations include: i) the lack of counterbalancing for the IB and AB task; ii) the failure to check whether participants interpreted the labels assigned to the stimuli presented in the same manner; and iii) that the chronic pain patients recruited did not possess a clinical diagnosis.

Most recently, Blaisdale-Jones et al. (2021) investigated AB and IB in chronic pain patients and healthy controls. AB were assessed using visual scanning methodology, while IB were assessed via an ambiguous paragraph recognition paradigm. The ambiguous paragraph recognition paradigm shares many similarities with the word completion task. Firstly, a series of paragraphs are presented, each with a unique identifying title (e.g., The road trip) and missing end word (e.g., "…Everything is fun until a car in the left lane swerves sharply and causes you to have a cr_ _ h). Participants are then asked to complete the missing end word of each paragraph, prior to the presentation of a comprehension question to check participants understood the details of the scenario. Secondly, following a short distraction task, the title of the ambiguous paragraphs is re-displayed to participants, accompanied with 4 alternative endings (2 pain/threat/illness-related, 2 non-pain/threat/illness-related). Participants rate the endings for similarity in meaning to the original scenario on a 4 point-scale (1 = very different in meaning, 4 = very similar in meaning). Findings revealed no between-group differences in various AB indices (i.e., latency, direction of first fixation, number of fixations, overall dwell time) or IB. That said, correlations to investigate the interrelationship between AB and IB showed that while ABs were weakly associated with IBs, little support for strong relationships between these variables were observed. Lastly, a significant relationship between pain intensity and IB were observed, indicating that individuals who suffer from higher levels of pain exhibit a tendency to interpret ambiguous information in a more pain-related fashion. Consequently, the authors concluded that while ABs to pain are 'ubiquitous', IBs warrant further investigation.

In summation, theoretical models have proposed insightful but also conflicting hypotheses regarding the interrelationship between cognitive biases and pain, with research findings described as mixed at best. To expand, the TIM and IFCF assign differing temporal relationships between AB and IB, with the TIM predicting that IB precedes AB whereas the IFCF speculates the opposite. Hence, further research is needed to directly test these theories by distinguishing whether AB informs IB or vice versa, which will have important theoretical implications for researchers examining cognitive biases in acute/chronic pain .

1.5 Implications of Studying Combined Cognitive Biases in Pain

Investigating attention, interpretation and memory bias in the field of chronic pain has a plethora of important clinical implications. Firstly, if a causal link can be established between attention, interpretation and memory bias then early screening combined with psychological interventions that aim to target and retrain these biases could help to reduce the development of chronic disability. Secondly, early screening would help to target these biases before they become deep-rooted, thus potentially minimising the short and long-term effects of pain. Thirdly, studying these biases can help us to gain insight into the etiology, exacerbation and chronification of chronic pain and provide the opportunity to explore whether these processing biases are vulnerability factors or are the result of long-term exposure to pain. Lastly, given that much research in this field has investigated these biases in isolation, exploring the effects of these different forms of bias together may help us to gain a more realistic understanding of the exacerbation of chronic pain. Indeed, as previous research indicates that information processing biases interact, influence one another and operate in a cyclical fashion (Hirsch et al., 2006; Van Ryckeghem et al., 2019), exploring more fully the role these biases play in the acute/chronic pain experience, and with more robust methodology (see section 1.6 below), should be a key consideration for future research (and thus the main focus of this PhD thesis).

1.6 Limitations of Current Research

The pain-related AB literature suffers from several important limitations. To recap, many studies use pain-related word stimuli within the scope of an AB task (for review see Schoth et al., 2012; Crombez et al., 2013). This is problematic as word stimuli require cognitive processing which limits their subsequent ecological validity and threat value (Dear et al., 2011). Considering the theoretical predictions of the TIM (Todd et al., 2015) this is important as threat value directly corresponds to the subsequent attentional processes displayed by an individual. Hence, pain-related pictorial stimuli should be used instead - given images possess higher ecological validity. However, while stimulus sets containing pain-related images are available (as mentioned

previously), including the IAPS (Lang et al., 1997; Lang & Bradley, 2007), GAPED (Dan-Glauser & Scherer, 2011) and PICS (pics.stir.ac.uk), these broad-topic databases often do not contain sufficient specific stimuli to investigate cognitive biases in pain, and/or do not all have data pertaining to the emotional properties of the stimuli (e.g. threat value and/or pain intensity discussed in Chapter 3), which are key limitations that need to be addressed in future research.

Secondly, studies investigating ABs in pain suffer from methodological inconsistencies that can contribute to both methodological heterogeneity and a lack of direct comparison with other studies (Chan et al., 2020). To expand, small sample sizes, use of differing experimental paradigms (e.g., emotional stroop vs. visual probe vs. visual search) and a lack of direct/continuous measures of attention are all contributory factors. Thus, further research is needed to investigate AB's using rigorous procedures/paradigms that can fully encapsulate the dynamic nature of attention (e.g., eye-tracking), as opposed to the use of existing paradigms that are only capable of providing a snapshot of attention allocation (e.g., emotional stroop or the visual probe task with button press methodology only).

With respect to IBs, it is well known that indirect measures suffer from limitations associated with demand characteristics and response biases. Direct measures are not devoid of criticism, however, with traditional paradigms (e.g., Homophones/Homographs) heavily criticised for a lack of appropriate stimuli and issues with words being associated with differing written/verbal frequencies (Schoth & Liossi, 2016). Indeed, the most recently developed paradigm – the AIBT (Heathcote et al., 2016) has limitations, such as the use of a forced-choice response format which requires participants to select one of two possible pre-determined interpretations. Whilst detailed fully in Chapter 2 (***section 2.3.2.4***), this is problematic as these interpretation options may not necessarily reflect the participants' own implicit interpretation of the scenario. Moreover, the lack of inclusion of filler scenarios could result in biased responses via demand characteristics and priming (e.g., towards pain interpretations per se). Hence, modifying the paradigm to enable participants to generate their own responses to each ambiguous scenario and including filler scenarios would increase the validity of the paradigm, and provide a more accurate measure of IB's. It should also be re-stated that while the small stimulus set used in the AIBT is suitable for

investigating pain conditions, treatment efficacy and associated psychological factors in youth (Heathcote et al., 2015; 2016; Lau et al., 2019), it is unknown whether said stimuli are suitable for use with adult populations.

Like limitations highlighted with respect to AB literature, the memory bias (MB) literature too suffers from critiques pertaining to methodological heterogeneity, due to discrepancies in retrieval instructions, variation in the time allocated for retrieval, use or non-use of distractor tasks and even the mode of presentation (for review see Chapter 2, ***section 2.4).*** Importantly, studies within the MB literature have predominantly focused on recall as the primary outcome measure of MBs, with little consideration of recognition. Recognition paradigms can be argued to be a better measure of MBs due to more efficient retrieval cues and the involvement of comparison processes between the available and stored information (Maratos et al., 2020). That said, regardless of whether focusing on recall or recognition, pain related MBs have not been assessed over time, with most studies employing immediate free recall tasks, and those that do employ delayed free recall tasks using short time intervals. Hence, to gain a more detailed understanding of pain related MBs (e.g., over the course of days/weeks) longitudinal research is needed to assess if and how MBs change over time.

Lastly, and as explained previously, a central tenet of the IFCF (Van Ryckeghem et al., 2019) is that cognitive biases interact and operate in a cyclical fashion to impact pain chronicity. Considering this, there is a need for more cross-bias studies to further understand the role, nature, and interaction between these differing forms of bias. Whilst recent research has made progress in measuring more than one bias in the context of a single study (e.g., Todd et al., 2016; Hughes et al., 2017; Schoth et al., 2018, 2019; Chan et al., 2020; Blaisdale-Jones et al., 2021), more needs to be done to incorporate each of the three main biases in future research.

Given the encompassing literature review and observed aforementioned limitations of current theory and research, clear rationale is provided for the aims and objectives of this PhD thesis.

1.7 Thesis Aims and Objectives

In sum, there is now evidence for the existence of attention, interpretation and memory biases in adults with chronic pain. However, it is important to acknowledge that research currently investigating the roles of these different forms of bias in pain is scant and of the research that does exist, findings can be considered as 'mixed' at best. Hence, the purpose of this PhD programme of research is to utilise a number of different experimental methodologies and paradigms to investigate the role of attention, interpretation and memory biases in non-pain, acute and chronic pain populations. Additionally, by utilising three different populations (non-pain group, acute pain group, chronic pain group) detailed insight into how the experience of pain influences these cognitive biases (and over time) can be achieved. The specific aims and associated objectives of this PhD are as follows:

Aim 1: To validate stimulus sets suitable for measuring pain-related attention and interpretation biases in Adults. The objectives include;

i) To validate pain-related images from broad-topic databases and gain measurements of their emotional properties (valence, arousal, threat value, pain intensity), to increase ecological validity and enable better investigation of AB.

ii) Developing an AIBT task using free and forced-choice response formats, and with filler (i.e., 'neutral' trials) suitable for use with adults to enable proper and rigourous investigation of IBs.

Aim 2: To examine whether the experience of pain influences attention, interpretation and memory bias by investigating these cognitive biases in: i) a pain-free sample and ii) a pain-free sample subjected to acute pain. With the specific objectives of;

i) Determining if attention and interpretation biases are both influenced by pain
ii) Determining if pain-related attention and/or interpretation biases influence the development of memory biases (including both recall and recognition biases).
iii) Determining if pain influences memory biases over time.

iv) Explore any relationships between attention, intepretation and memory biases as a consequence of acute pain experience.

Aim 3: To investigate combined cognitive biases in a clinical sample (e.g., chronic pain). In relation to this, the objectives is to;

i) Determine whether individuals with chronic pain display interpretation and memory biases for pain-related information compared to their pain-free control counterparts (measuring attentional biases in this sample was beyond the scope of this thesis, due to the suspension of face-to-face data collection as a consequence of the COVID-19 pandemic).

The above aims will elucidate the extent to which individuals with pain display cognitive biases for pain-related information compared to pain-free counterparts, allowing for advancement in pain theory (with respect to whether AB precedes IB or vice-versa), and tools to investigate pain biases/intervention efficacy. Thus, this body of research will provide a significant and original contribution to knowledge and, additionally, could inform new paradigms used in the assessment of pain management programmes.

Chapter 2 **Methodology**

This chapter will begin by reviewing the main cognitive techniques used to investigate attention, interpretation, and memory biases in the field of pain. Cognitive biases have been assessed using a plethora of differing experimental paradigms. For instance, threat-related Attentional Bias (AB) has been examined using emotional stroop, spatial cueing, visual search, visual probe and free-viewing methodologies (for a review see Chan et al., 2020). Interpretation Bias (IB) has been measured via the homographic/homophonic response task, word generation task, incidental learning task and the ambiguous scenarios task (for a review see Schoth et al., 2018). Memory Bias (MB) on the other hand, has been predominantly measured using modified free recall tasks (for review see Pincus & Morley, 2001; Schoth & Liossi, 2020), and to a lesser extent recognition tasks (e.g., Grisart, 2007). Considering the wide range of available paradigms, it is important to evaluate the strengths and limitations of these experimental methodologies when measuring cognitive biases in pain; therefore, a review of techniques to investigate these differing cognitive biases is the first focus of this Chapter.

Various techniques have also been used to experimentally induce pain. For instance, pain can be induced via mechanical (e.g., pinprick), chemical (e.g., capsaicin), electrical and thermal stimulation (e.g., cold, for review see Reddy et al., 2012). Given that questions have been raised regarding the comparability and reliability of these methods in previous research (for a review see Staahl & Drewes, 2004), the second focus of this chapter will be to review the main pain induction methods used in humans. This chapter will culminate in justification for the experimental methodologies used in this PhD research to measure cognitive biases and experimentally induce pain.

2.1 Methodology Review Approach

To identify experimental paradigms used within the field of pain to measure attention, interpretation and memory bias, studies were identified by searches of Google Scholar, Medline, Psych INFO and Psych Articles. The search terms for each form of bias are outlined below. For cognitive paradigms to be included in the methodology, they had to:

i. Be available in English Language.
ii. Be used to examine attention, interpretation, or memory bias within the context of pain (acute or chronic).
iii. Use the paradigm with a sample of adults ((≥ 18 years old).
iv. Be an experimental study using a paradigm to measure cognitive bias(es), or a systematic review/meta-analysis of experimental paradigms used within the context of pain (acute or chronic).

With respect to the inclusion of pain induction techniques, the only permutation was that the techniques had to have been performed on human participants.

2.1.1 Search Terms for Attentional Bias

Search terms included ‘attention*’ or ‘attentional bias’ or ‘hypervigilance’ AND ‘emotional stroop’ or ‘spatial cueing’ or ‘visual search’ or ‘dot-probe’ or ‘visual-probe’ or ‘free viewing’ or ‘eye-tracking’ or ‘eye-movement’ or ‘attention tracking’, intersected with the term ‘pain*’.

2.1.2 Search Terms for Interpretation Bias

Search terms included ‘interpretation*’ or ‘interpretation bias’ or ‘endorsement bias’ AND ‘homograph or ‘homophone’ or ‘word stem completion’’ or ‘ambiguous scenario’ or ‘incidental

learning' or 'direct interpretation bias or 'indirect interpretation bias', intersected with the term 'pain*'.

2.1.3 Search Terms for Memory Bias

Search terms included 'recall*' or 'recognition*' or 'memory*' AND 'enhanced memory' or 'impaired memory' or 'memory impairment' or 'attentional cost' or 'hypervigilance' or 'working memory' or 'signal detection' or 'd-prime' or 'criterion c', intersected with the term 'pain*'.

2.1.4 Search Terms for Pain Induction Methods

Search terms included 'chemical' or 'thermal' or 'mechanical' or 'electrical' AND 'induction' or 'stimulation' or 'manipulation', intersected with the term 'pain*'.

2.1.5 Additional Details

To attempt to identify any other attention, interpretation, and memory bias paradigms that were not included within the methodological review, an examination of the reference lists of relevant articles was conducted and published systematic reviews/meta-analyses were identified and read.

All literature searches were conducted between January 2019 and August 2019, and subsequently updated in September 2020.

2.2 Cognitive Paradigms used to Investigate Pain-related Attentional Biases

Below follows a brief review of all the key paradigms that have been used in previous research to measure AB in pain.

2.2.1 Emotional Stroop

The most common early paradigm used to measure AB in the context of pain was the modified Stroop colour naming task (for review see Roelofs et al., 2003). This task involves presenting emotionally salient words (i.e., affective and/or sensory pain words) and neutral words in different colours (e.g., Stabbing, Piercing, Sharp etc.). Participants are asked to identify the colour of the words as quickly as possible, with response times recorded (see **Figure 2.1**). It is predicted that the emotive content of salient words will interfere with the colour naming task, resulting in a longer response time. Hence, applied to the field of pain, it is predicted that participants will take longer to name the colour of pain-related word stimuli, as opposed to neutral stimuli. Evidence has been mixed, however, with some studies supporting the notion that chronic pain patients selectively attend to affective and sensory pain stimuli (Roelofs et al., 2003; Duschek et al., 2014), while others have reported no such findings (Pincus et al., 1998; Roelofs et al., 2005).

Unlike self-report measures, the emotional Stroop is objective and unobtrusive. A key strength of this paradigm is that it has helped to answer key questions about cognitive processing. For example, how do chronic pain patients perform on a focal task when irrelevant emotional information is presented, particularly when sensory and/or affective words are used which may match the underlying pathology of the patient? That said, this paradigm is considered a weak measure of AB as it is unable to distinguish between the various components of AB. To expand, it is unclear whether difficulty disengaging (from the pain-related stimuli) or attentional avoidance (i.e., allocating attention away from the pain-related stimuli) is responsible for the observed delay in response time. Indeed, difficulties disengaging via looking at the word as opposed to the colour, and avoidance via not looking at the pain-related stimuli, would both cause slowed responding.

Hence, it may be unsuitable to assume that delayed Response Times (RT) to name the colour of pain-related word stimuli reflect an AB towards pain-related information. Indeed, Algom et al., (2004) demonstrated in a series of experiments that the emotional Stroop task simply measures a threat-driven generic slowdown as opposed to the mechanisms of selective attention. To illustrate this, they found that reading, lexical decision and colour-naming were all slower with emotional words, and that changes to the salience of the words did not impact this delay.

Considering the above, cognitive paradigms that can differentiate between the key components of AB are therefore preferential to simplistic measures of attention like the emotional stroop paradigm (where components of disengagement compared with avoidance cannot be untangled).

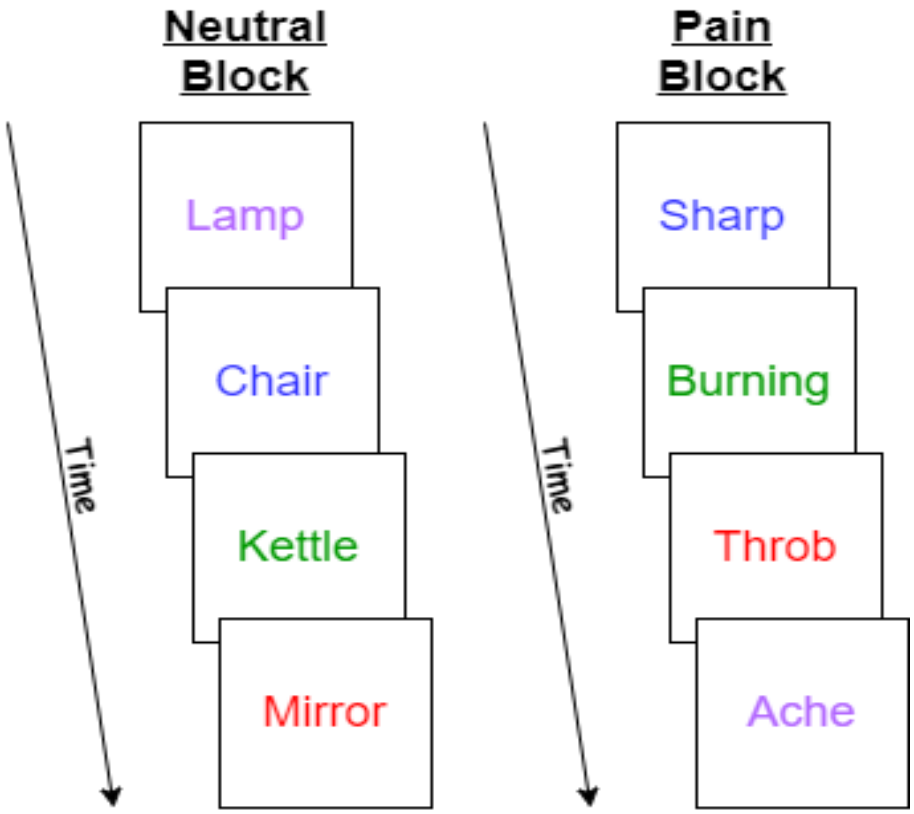


Figure 2.1: **Example Blocks of Neutral and Pain Stimuli in an Emotional Stroop Task. The Task of the Participant is to Name the Colour the Word is Printed in.**

2.2.2 Spatial Cueing Task

The spatial cueing task (also known as the Posner Spatial Cueing Task, Posner, 1980) has been a widely used tool for investigating AB. In recent years, the task has been modified to measure attentional processing in chronic pain patients (Chapman & Martin, 2011; Van Ryckeghem et al.,

2013). In this task, participants are first presented with a single cue stimulus, which is either pain-related (e.g., a facial expression depicting pain) or neutral (e.g., a neutral face) at one of two possible locations on the screen (e.g., left or right). After a short interval, the cue disappears and a target either appears at the previously cued location (congruent trial), or at the opposite location (incongruent trial). Typically, in 80% of trials the cue is pain-related and in 20% of the trials the cue is neutral. Participants are instructed to respond as quickly and accurately as possible to the identity and location of the target (see **Figure 2.2**). A cue validity index is calculated to determine whether AB has been found. This involves subtracting response times on congruent trials from response times on incongruent trials. A greater cue validity index on trials with a pain-related cue, relative to a neutral cue, suggests an AB towards pain-related information.

Despite the paradigm's popularity within psychopathology (e.g., anxiety), few studies have utilised this paradigm in the field of pain. This stated, Chapman and Martin (2011), using a word cue version, found that participants with Irritable Bowel Syndrome (IBS) exhibited faster engagement with positive words compared to their healthy counterparts. Chapman and Martin (2011) further observed that self-report measures of pain were associated with increased reporting of somatic symptoms and sick leave taking. Moreover, Schrooten et al., (2012) recruited a sample of healthy participants to examine whether AB to pain signals is displayed when pursuing a concurrent non-pain goal. Healthy participants were split into a goal and control group. To increase the importance of goal pursuit, monetary reward and punishment (electro cutaneous stimuli) were performance dependent. Using a spatial cueing task where pain and neutral cues were presented to participants, Schrooten et al., (2012) found that AB to pain signals were only present in the control as opposed to the goal group. Hence, demonstrating that AB to pain signals can be inhibited in healthy participants when one is given a current salient, but non-pain goal to pursue. Most recently, Van Ryckeghem et al. (2012) conducted the first study using the spatial cueing task with pain cues (signalling upcoming pain) as a means of assessing selective attention in a sample of chronic pain patients. Here, participants were required to discriminate probe identity (i.e., : or "), which was preceded by a pink or blue square cue at the same or opposite location. Using a differential classical conditioning procedure, the colour of the cues was counterbalanced, one of which signalled pain via electro cutaneous stimulation, while the other did not. While no overall effect of AB towards

pain-related information was observed, an AB towards pain-related information was found to be related to current disability and current pain severity in chronic pain patients. Hence, these studies highlight the utility of this paradigm in better understanding the effects of pain-related information on processes of spatial attentional bias in pain patients.

That said, there are several limitations of this paradigm. For instance, only one threatening stimulus is presented at any given time in the spatial cueing task. Thus, it is difficult to test effects of competition on attentional processing. To expand, in visual-search and visual-probe tasks, two or more stimuli are presented at the same time which induces competition amongst attentional resources. This is important as research suggests that threat only modulates attention when there is competition between threatening and non-threatening stimuli (Matthews & Mackintosh, 1998; Simione et al., 2014), or that these effects are much smaller in the absence of pairing threatening with neutral stimuli (White et al., 2011). Indeed, some researchers also argue that this paradigm may not provide an unambiguous measure of attention. For example, Hayward and Ristic (2013) found that while previous research attributes findings to spatial attention (i.e., orienting), the parameters of the task induce tonic alertness (i.e., continuous internal arousal) and potentially voluntary temporal preparation which influence the observed attentional effects.

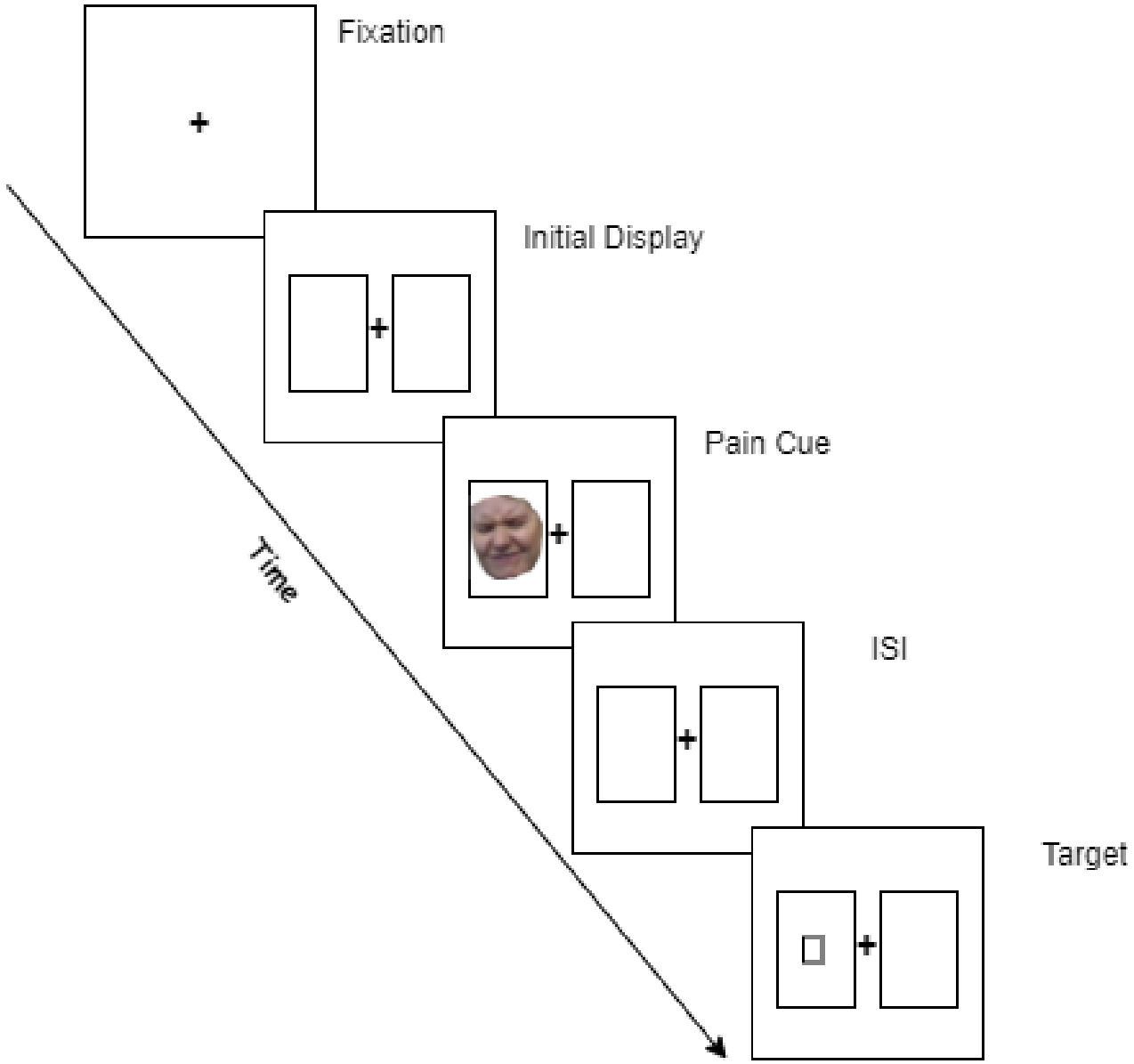


Figure 2.2: **Example Congruent Pain Trial in the Posner Spatial Cueing Task. The Task of the Participant is to determine the location of the target via motoric responding.**

2.2.3 Visual Search Paradigm

Another popular method to investigate spatial AB is the visual search paradigm. In a standard version of the visual search paradigm, participants search for a target amongst a number of distractor items. The total number of items is known as the set size. On a percentage of the trials, typically 50%, a target is presented. On the other trials, only the distractor items are presented. Participants are required to make one response to indicate that they have located the target and another to indicate if no target has been found. Typically, measures of RT and accuracy are recorded. Studies where RT is the primary measure of interest typically analyse RT as a function of set size. This produces two functions – one for trials where the target is present and one for trials whether the target is absent. In emotion research, speeded responses to detecting threat-related faces presented in an array of neutral faces, compared with neutral faces presented in an array of threatening faces, is thought to demonstrate facilitated engagement to threat. Whereas slower RTs to detect neutral faces embedded in an array of threatening faces, as opposed to threatening faces embedded in an array of neutral faces, would demonstrate difficulty disengaging from threat (Cisler & Koster, 2010).

Applied to the field of pain, researchers have developed novel visual search paradigms (Veldhuijzen et al., 2006; Notebart et al., 2011; Schoth et al., 2015). In such studies, trial events are typically as follows; first, a fixation cross appears in the centre of the computer screen. Once participants fixate on the cross, it disappears and is replaced by images depicting different emotions in a circular array (see **Figure 2.3**). Target-present trials include one target image (e.g., pain face) and 7 identical distractor images (e.g., neutral face). Whereas target-absent trials include 8 identical distractor images. Stimuli are often presented in two blocks, these include emotion-target trial blocks (one emotional expression embedded among 7 neutral faces) and neutral-target trial blocks (one neutral expression embedded among 7 pain faces).

Studies employing this paradigm within the field of pain have yielded mixed results. For instance, Veldhuijzen et al. (2006) conducted two experiments to examine the effect of pain processing on attention capacity during visual search, the findings of each experiment revealed that pain did not significantly affect task performance. Conversely, Notebaert et al., (2011)

observed AB using visual search. Healthy volunteers were randomly allocated (by lottery) to either a pain-control or comparison group. Those in the pain-control group were observed to exhibit hypervigilance to pain. Moreover, using eye-tracking technology, Schoth et al., (2015) found that relative to healthy controls, participants with chronic headache displayed a greater proportion of initial fixations to target pain expressions when the pain expressions were presented in displays containing neutral faces (i.e., distractors).

Despite the mixed evidence observed above, a strength of the visual search paradigm is that unlike the emotional Stroop and posner spatial cueing tasks, multiple stimuli are presented at any one-time creating competition for attentional resources, which has helped to test competing theories of selective attention. Furthermore, this paradigm can differentiate between processes of attentional orienting and disengagement (Derakshan & Koster, 2010). However, Kristjanson (2015) has raised concerns over the use of RT in the study of search, arguing that the slopes of RT by set size are ambiguous. Additionally, the task has also been criticised since participants are instructed to search for a particular face (e.g., pain, neutral). Hence, Smith et al., (2006) posit that AB effects arising are instructed by the research and are thus goal dependent.

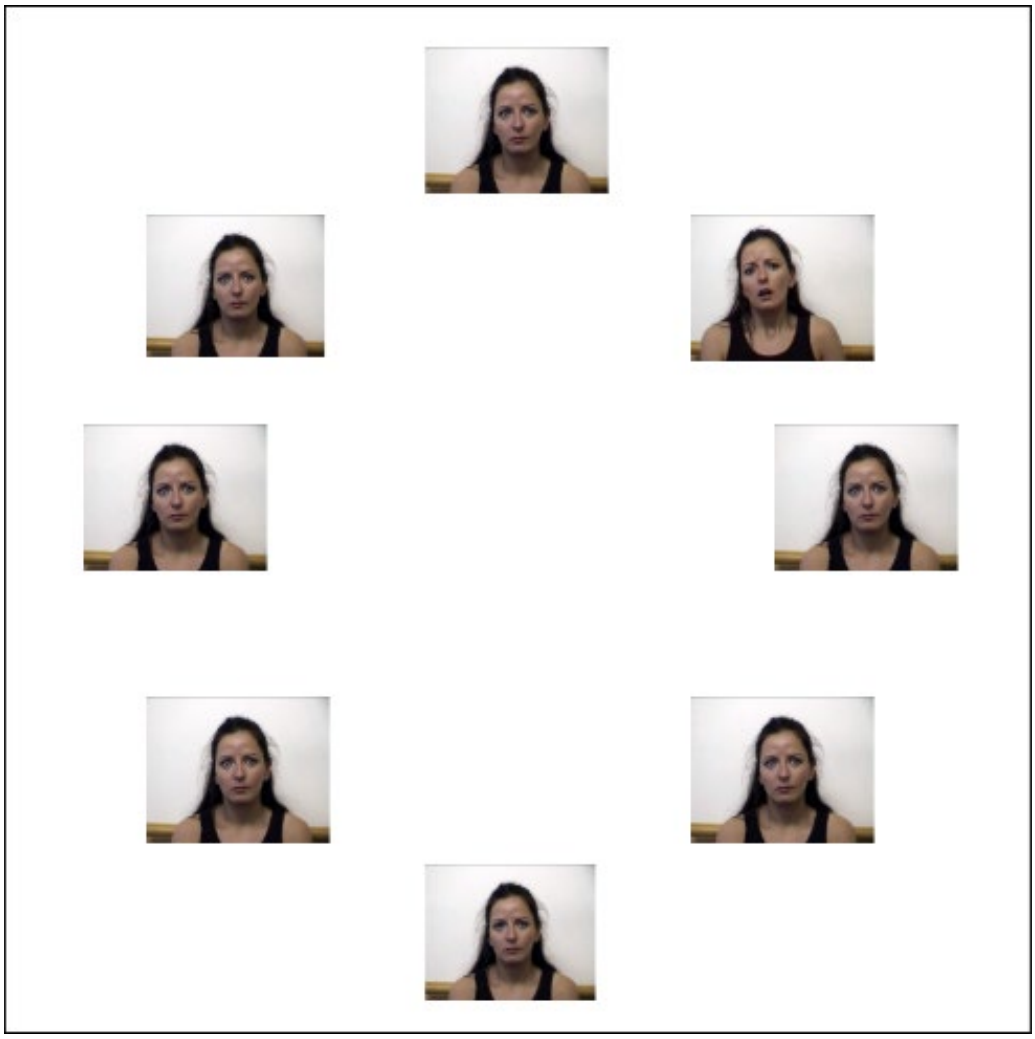


Figure 2.3: **Example Target-Present Trial in an Emotional-Target block (one pain expression embedded among 7 neutral faces). The task of the participant is to identify the target face (pain face in this example).**

2.2.4 Visual Probe Task

Arguably, the most used paradigm to measure AB in the field of chronic pain is the visual probe task (also known as the dot-probe detection task, Todd et al., 2018). The visual probe task was originally developed by MacLeod et al. (1988) and has traditionally been used to investigate AB in various forms of psychopathology, including social anxiety (for review see Bantin et al., 2016), depression (for review see Winer & Salem, 2016) and eating disorders (for review see Faunce et al., 2002). The visual-probe task is a computerised paradigm, of which trial sequences are typically as follows: first, a fixation cross (+) appears in the centre of the computer screen. After a set time period this disappears and two stimuli, one threat-related and one neutral, appear simultaneously on the computer screen. Applied to the field of pain, the threat-related stimulus is replaced with a pain-related stimulus. These stimuli are then displayed for a predetermined length of time (e.g., 500ms). Following this, both stimuli disappear and a probe (e.g., *) appears in the location of one former stimulus (see **Figure 2.4**). If the probe appears in the former location of the threat/pain-related stimuli this is classed as a 'congruent' trial, whereas if the probe appears in the former location of the neutral stimulus this is classed as a 'incongruent' trial. Participants are instructed to discriminate probe identity as quickly and accurately as possible using a keyboard or response box. Participants are typically given a set amount of time to respond (e.g., 3000ms). If no response is made within this time, the probe display is offset, and the next trial begins.

Generally speaking, RT is faster to probes that appear in the attended region of the screen compared to the unattended region. Hence, this provides a measure of where visual attention has been allocated during probe presentation. Speeded responses to congruent trials, relative to incongruent trials, indicate enhanced attentional allocation to the threat/pain-related stimulus and/or reduced attentional allocation to the neural stimulus. Likewise, delayed responses to congruent trials, relative to incongruent trials is indicative of reduced attentional allocation to the threat/pain-related stimulus and/or enhanced attention to the neutral stimulus. RTs can also be averaged for both congruent and incongruent trials to calculate an index score of AB. To calculate an AB index score, the average RT for incongruent trials is subtracted from the RT for congruent trials. A positive score on the bias index indicates a shift of attention towards the location of the

threatening/pain-related stimulus, whereas a negative score indicates a shift of attention away from the threatening/pain-related stimulus towards the neutral stimulus (indicative of avoidance). A score of 0 indicates no evidence of bias or avoidance.

Recent systematic-review and meta-analytic evidence supports the utility of the visual-probe task in detecting pain-related AB. Indeed, Schoth et al., (2012) conducted a meta-analysis of ten studies using visual-probe methodology and found evidence to suggest that chronic pain patients display significantly greater ABs towards pain-related information compared to their healthy, non-pain counterparts (*Hedges g = .36).* Moreover, the authors also examined the time-course of AB, with significant biases observed during the initial orienting of attention (*Hedges g = .29)* and a larger bias observed during attentional maintenance (*Hedges g = .42)*. More recently, Todd et al., (2018) conducted a systematic review and meta-analysis of 52 visual-probe studies with a total of 4466 participants grouped into the following categories based on their pain experience: chronic pain, acute pain, anticipating experimental/procedural pain, social concern for pain or healthy people. Results revealed a significant but small bias towards pain words and pictures in chronic pain patients, but not in those with acute pain, anticipating experimental/procedural pain or healthy controls. Further, follow-up analyses revealed an AB towards sensory pain-words (e.g., Burning) in the chronic pain group and the acute pain group, but not in the other groups, while no significant ABs towards affective pain words (e.g., Torturing) were observed in any group. Hence, the authors concluded that while the meta-analysis supports the notion that pain patients display an AB towards sensory-pain words, future research should carefully consider task design to optimally measure pain-relevant AB.

The use of the visual-probe paradigm has multiple advantages over the other paradigms outlined above. The visual-probe task can easily be modified to present pictorial stimuli (e.g., facial expressions), which have become increasingly popular in AB tasks as they possess greater ecological validity than word stimuli. Further, as competition among stimuli has been postulated to be a prerequisite for AB to emerge (Bar-Haim et al., 2007), the simultaneous presentation of threat/pain-related and neutral stimuli is another notable feature. Most importantly, as evidenced in the findings of Schoth et al. (2012), stimulus presentation lengths are controlled by the

researcher which enables the exploration of the time-course of AB. For instance, presentation lengths can be set to measure biases during the early (i.e., 500ms) and later (e.g., 1500ms) stages of attentional processing.

Nevertheless, there are limitations associated with the use of this paradigm. Firstly, RT is an indirect measure of AB and assumes that gaze location corresponds to motor (i.e., usually manual) responses, which is not always the case. Secondly, this paradigm only provides a snapshot of attentional deployment and fails to capture any shifts in attention that may occur within the duration of each trial (Armstrong & Olatunji, 2012). Thirdly, Mogg and Bradley (1999) highlight that probe discrimination versions of the task are high in cognitive load, with participants producing 3x as many errors and being 200ms slower in their responses. Hence, rather than probed discrimination, a more objective and accurate measure of attentional processing is needed to be able to distinguish between the three core components of attentional processing: orientation, disengagement, and avoidance.

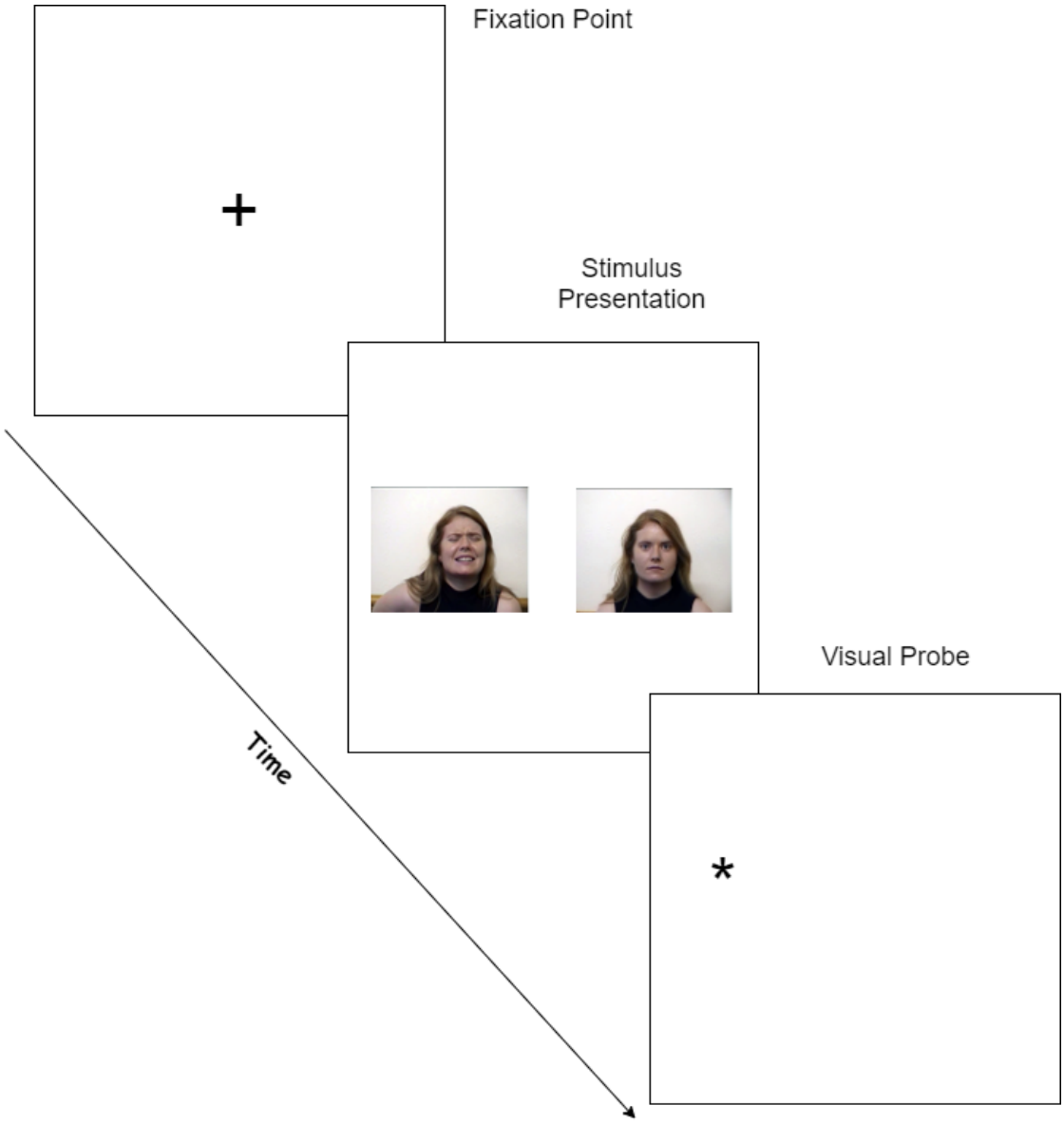


Figure 2.4: **Example Congruent Trial in a Visual Probe Identification Task. The task of the participant is to identify the location of the visual probe) as quickly as possible.**

2.2.5 Visual Probe Task and Eye-Tracking Technology

Given the limitations of using the visual-probe task alone, researchers have now begun to use eye-tracking technology in conjunction with visual-probe methodology (e.g., Fashler & Katz, 2014, 2016). Eye-tracking provides a continuous measure of eye-movements in real time and tracks gaze behaviour of one (monocular) or both (binocular) eyes. Hence, it provides a direct measure of overt attentional deployment (Bogels & Mansell, 2004). When used in conjunction with the visual-probe task, the determinants of RT can be clarified, for example, does the RT data indicate vigilance to the threat/pain-related stimuli, avoidance of the threat/pain-related stimuli, or both? Eye-tracking provides the possibility of measuring numerous processes of attention, including orientation (reflected by the direction and latency of first shift in gaze), engagement (reflected by the direction and latency of fixations and dwell time) and disengagement (reflected by dwell time and fixations away from a particular stimulus).

In recent years, research has found eye-tracking indices to be more reliable than RT indices of AB even when a very small number of trials are used (Price et al., 2015). Further, Christiansen et al., (2015) found that adopting more personalised stimuli and incorporating eye-tracking technology can help to increase the internal reliability of the visual-probe task. Lastly, within the field of pain, researchers have shown that individuals with chronic pain fixate and visit injury-related images more often and exhibit longer average visit durations, as compared to individuals without chronic pain (Fashler & Katz, 2016). This highlights the utility and effectiveness of incorporating eye-tracking technology during a visual probe task. Nevertheless, a recent systematic review of the eye-tracking evidence found that studies which incorporated eye-tracking technology with visual-probe methodology often found no significant differences in relation to reaction time (Chan et al., 2020). Hence, it is questionable whether visual-probe methodology with manipulations of stimulus presentation length and congruency are needed, given the benefits of using free viewing eye-tracking paradigms. These paradigms provide continuous data over the time course of stimulus presentation (i.e., 3000ms to explore initial orienting as well as processes of attentional maintenance and/or disengagement). Further, incorporating reaction time via button press methodology only has practical value for exploring motoric threat slowing.

2.2.6 Eye-tracking and Free viewing Paradigms

Recent advancements in eye-tracking technology allow for experimental designs that examine overt attentional deployment over the time course of stimulus presentation, which are argued to produce more reliable data. For instance, Chan et al., (2020) included a total of twenty-four eye-tracking studies in their systematic review of the AB and pain literature, of which 13 used free-viewing methodology, 12 visual-probe and 1 visual-search. Notable strengths of the free-viewing paradigms included were the ability to distinguish between various components of attentional processing (orienting, engagement, disengagement), the concurrent presentation of multiple stimuli with various presentation lengths (ranging from 1000ms to 8000ms) and the increased flexibility in measuring ABs.

Trial event sequences for free viewing tasks are typically as follows; firstly, a fixation cross is presented in the centre of the screen for a pre-determined length of time (e.g., 500ms) or is used as a prompt to initiate automated stimulus presentation once fixated upon. Secondly, a pair of images (one pain-related, one neutral) are presented simultaneously on screen for 3000ms. Thirdly, a blank screen or inter-stimulus interval is then presented prior to the commencement of the next trial (see **Figure 2.5**). During these trial events, eye-tracking technology records a vast array of early and later attentional indices. However, much like the visual-probe task, studies employing a free-viewing paradigm vary considerably in their methodology. For example, studies have used varied stimulus presentation lengths (e.g., 1000ms; Mahmoodi-Aghdam, 2017), stimulus types (e.g., word stimuli; Lee et al., 2019), and manipulated threat via numerous means (e.g., via prior information manipulation, image presentation or pain signalling). This is problematic as it shows that methodologies within the field of pain and attention are heterogenous. Considering this, it is unsurprising Chen et al., (2020) concluded in their systematic review that results regarding threat and gaze biases are not yet conclusive. Hence, further research employing a more standardised approach to investigate AB over the entire course of stimulus presentation is needed.

Despite limitations of free-viewing paradigm design, however, a key advantage of studies employing this methodology with longer stimulus presentation lengths is that they can obtain a variety of AB measures. These include initial orienting (e.g., first fixation proportion/latency),

attentional engagement (e.g., total fixation count, total visit count), attentional disengagement (e.g., fixation/visit count, total gaze duration) and attentional maintenance (e.g., duration of first fixation/visit, average fixation/visit duration, total gaze duration). This enables all aspects of attentional processing of pain-related information to be investigated in a single study (Skinner et al., 2020).

Free viewing with eye-tracking technology was therefore the methodology used in the current thesis research (e.g., Chapter 5) to assess whether pain and/or injury-related stimuli influence the time course of ABs in participants subjected to acute experimental pain.

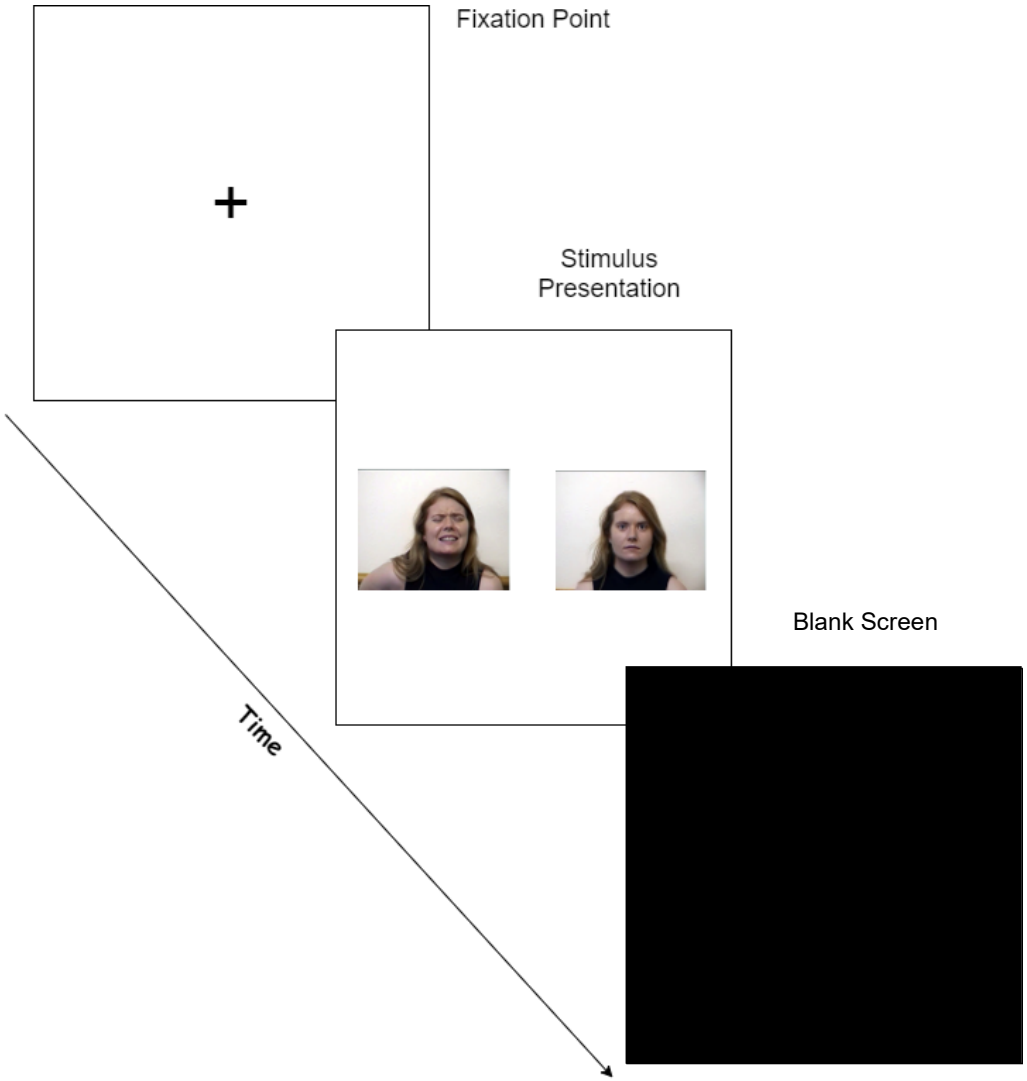


Figure 2.5: **Example Trial in a Free-Viewing Task. The task of the participant is to view the images in any manner that they wish.**

2.3 Cognitive Paradigms Investigating Pain-related Interpretation Bias

The IB literature is comprised various stimulus types and assessment methods (for full review see Schoth & Liossi, 2017). To expand, stimuli can be organised into three main categories: ambiguous words (e.g., Homophonic Response Tasks, Homographic Response Tasks, Word Stems Completion Tasks and Sentence Generation Tasks), ambiguous images (e.g., Incidental Learning Task), and ambiguous scenarios (e.g., Adolescent Interpretation Bias Task). With respect to measurement methods, direct and indirect measures of IB have been employed. Direct methods attempt to measure explicit IBs, based on the conscious cognitive processing of ambiguous stimuli (e.g., Word Stem Completion – number of pain/non-pain completions). Whereas indirect methods attempt to measure implicit IBs, that is, the unconscious and automatic processing of stimuli (e.g., Incidental Learning Task – response time) for review see Chapter 1, section 1.4.2). Below follows a brief review of indirect and direct measures of IB.

2.3.1 Indirect Measures of Interpretation Bias

2.3.1.1 Incidental Learning Task (Ambiguous Images)

A recently developed paradigm to measure implicit IBs in pain is the Incidental Learning Task (see Khatibi et al., 2014, 2015). This task provides an indirect measure of IB, inferring bias via behavioural response patterns (i.e., RT). The task typically consists of a learning phase and a test phase. In the learning phase, participants are presented with pictures displaying positive (e.g., happy) or negative (e.g., painful) facial expressions in the centre of the computer screen. These types of facial expression are predictive of the location of a subsequent target cue (e.g., 'H'). For example, positive facial expressions predict targets on the left side of the screen and negative facial expressions predict targets on the right side of the screen. This occurs for 80% of trials; however, the opposite is true 20% of the time. Participants are asked to indicate the location of a target (i.e., left or right) as quickly and accurately as possible using a response box (see **Figure 2.6**).

The test phase involves the presentation of neutral facial expressions followed by targets appearing with equal frequency on the left and right side of the screen. An IB is evident when, following the neutral facial expressions, participants respond faster to target cues in the location predicted by the 'relevant' emotive facial expression (e.g., Happy/Painful). To expand, faster responses to targets in the location predicted by negative (i.e., painful) facial expressions is indicative of a negative IB. However, faster responses to targets in the location predicted by positive facial expressions is indicative of a positive IB.

Few studies have tested this paradigm in the field of pain. Khatibi et al., (2014) conducted the first published study using this paradigm with morphed facial expressions to measure IBs in healthy participants split into high and low catastrophising groups. High pain catastrophisers were found to exhibit speeded responses following morphs to targets at the location predicted by a painful expression. However, when threatening or non-threatening contextual cues were presented, there was no evidence of an IB. Thus, suggesting the above is reflective of a pain, not threat bias. However, Todd et al., (2016) measured AB and IB in healthy participants using visual-probe and incidental learning paradigms respectively and found no relationship between AB and IB, and that IB was not influenced by threat or associated with pain. Yet, using a clinical sample of chronic pain patients, Khatibi et al. (2015) found that relative to controls, these patients showed a greater bias towards interpreting ambiguous faces as painful. Additionally, those with higher scores on self-report measures of fear of pain and pain catastrophising were found to be more likely to interpret ambiguous faces as painful. That said, while a significant relationship was observed for IB and pain catastrophising, the same was not observed for pain-related fear. Nevertheless, this study provided strong evidence to suggest that individuals with chronic pain display an IB for ambiguous faces, and that pain catastrophising is associated with an increased tendency to interpret ambiguous information in a negative manner.

A key strength of the incidental learning paradigm is that it avoids the pitfalls associated with direct measures of IB in relation to their susceptibility to self-presentation biases (Hirsch & Mathews, 1997), including demand characteristics and response biases (Khatibi et al., 2014). However, Schoth and Liossi (2016) criticise the use of morphed facial expressions for lacking

ecological validity. This is because these stimuli may appear unnatural and unlike facial expressions viewed in everyday life. Moreover, there are also limitations associated with inferring interpretations from behavioural response patterns; namely, reaction time measures can be argued to not possess sufficient sensitivity to detect IB effects (Todd et al., 2016). Hence, using a more direct method of IB would avoid the pitfalls associated with this indirect measure of IB.

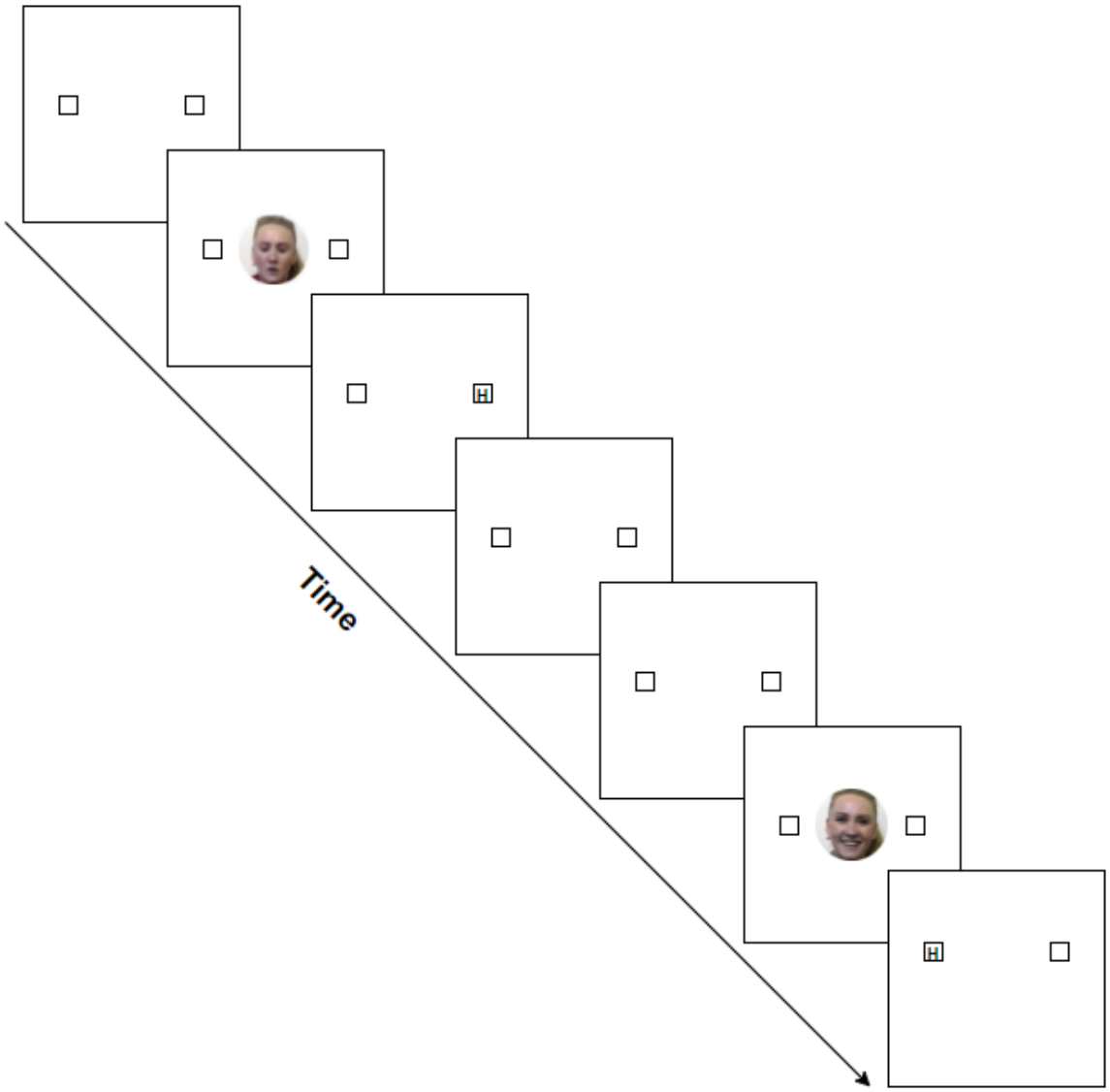


Figure 2.6: **Example Trial in the learning phase of the Incidental Learning Task. The task of the participant is to identify the location of target cue as quickly as possible.**

2.3.2 Direct Measures of Interpretation Bias

2.3.2.1 Homophonic Response Task (Ambiguous Word)

Historically, the Homophonic Response Task was one of the most popular methods of measuring IB. In this task, spoken homophones (i.e., words with different spellings but the same pronunciation), with threatening and neutral associations are presented (e.g., Pain vs Pane). Participants are typically asked to note down their interpretation of the word upon hearing it (Pincus et al., 1996). IB is quantified by a greater number of ambiguous homophones being interpreted in a pain and/or illness-related fashion, relative to the number of ambiguous homophones interpreted in a benign/neutral fashion.

While a notable strength of this paradigm includes it being simple to administer, the task does suffer from several major shortcomings. To expand, Simpson and Krueger (1991) highlight that the threatening and neutral associations of the same homophones often have varying written and verbal frequencies of use. The homophones 'pain' and 'pane' illustrate this. Participants, irrespective of whether they suffer from chronic pain or not, may be likely to interpret this spoken homophone as 'Pain' due to the word possessing a higher written and verbal frequency of use. Consequently, this paradigm suffers from having a small number of appropriate stimuli available (Schoth & Liossi, 2016). A further limitation of this paradigm, particularly when used in clinical research, is that disorder-relevant homophones are likely to be more familiar to patients as opposed to healthy participants. That said, studies have attempted to address this by recruiting additional participant groups (see Pincus et al., 1998) who are also familiar with these disorder-relevant words (e.g., health care professionals), to see if patients show an increased bias relative to this group.

2.3.2.2 Homographic Response and Sentence Generation Tasks (Ambiguous Word)

Researchers have also used Homographic Response Tasks (also known as the Ambiguous Cues Task or the Single-Word Associate Homographic Response Task) as a direct measure of IB (McKellar et al., 2003; Vancleef et al., 2016). This task involves presenting participants with

written homographs (i.e., words spelt the same but with different meanings e.g., punch - hit, punch - drink), and asking them to note down the first word(s) that come to mind that they can think of related to it. Typically, independent coders then categorise the response words into a threat-related category or a neutral category. IB is quantified as the relative difference between the number of words categorised as threat-related versus neutral (e.g., see Pincus et al., 1994; 1996). A variant of this task, the Sentence Generation Task, also uses homographs as stimuli to measure IBs (see Schoth et al., 2018, 2019). In this task, participants are instructed to formulate a short sentence including the homograph. Like the process above, independent coders categorise the sentences as either threat-related or neutral.

A strength of the homographic response and word generation tasks is that they are easy to administer. That said, these tasks may be subject to demand characteristics as participants may not necessarily provide the first responses that enters their mind. Similar to the limitations of the Homophonic Response Task, homographic words often have multiple connotations, some of which may be more dominant than others (Nelson et al., 2004). Hence, this raises the question as to whether paradigms utilising ambiguous homophones are suitable for measuring IBs.

2.3.2.3 Word Stem Completion Task (Ambiguous Word)

A further direct IB measure is the Word-Stem Completion task (Edwards & Pearce, 1994; Griffith et al., 1996). This task involves presenting participants with three letter word stems (e.g., Hor _ _ _ _ _). Participants are asked to complete the word stem with the first word(s) that enter their mind, which may be threat-related (e.g., Hor***rible***) or neutral (e.g., Hor***izons***). Applied to the field of chronic pain, word stems that can generate pain-related or neutral responses are used (e.g., Ten _ _ _; Ten***der*** or Ten***nis***). Independent judges are then used to categorise participant responses as either pain/illness-related or neutral.

Schoth and Liossi (2016), however, argue that subjectivity may exist in the independent judging procedure. To expand, participants may respond with homophones (e.g., Sharp) which have positive (i.e., sharp-clever) and negative (i.e., sharp-pain) connotations. Mueller and Thanasuan (2014) also highlight that word frequency and length influences participants responses

to this paradigm. That said, a strength of this paradigm is that there are a limited number of valid responses, which makes it easy to categorise pain/illness-related and neutral answers (Schoth & Liossi, 2016).

2.3.2.4 Ambiguous Scenarios Task (Ambiguous Scenarios)

Most recently, to overcome limitations associated with the above direct IB measures, ambiguous scenarios have been used to measure IB in adolescents with chronic pain (Heathcote et al., 2015, 2016; Lau et al., 2019). Heathcote et al. (2015) developed a novel Adolescent Interpretation Bias Task (AIBT), which entailed presenting adolescent participants with a series of ambiguous scenarios in the centre of the computer screen. For example;

"Someone kicks a ball and it hits you in the face. In the mirror you see your face is covered in…"

The situation is ambiguous as there are at least two possible solutions that reflect different interpretations. Participants are instructed to read the scenario and imagine themselves in that situation, prior to being offered a solution that completes the scenario in a negative manner (e.g., pain-related, **blood**) or benign manner (i.e., non-pain related, **mud**). Participants then rate how likely each solution was, or was not, to enter their mind from 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). Once this has been completed for all scenarios, participants are presented with the same scenarios again and are asked to rate their belief that each interpretation would be a true reflection of reality (i.e., whether that would actually happen in the scenario).

While studies using this paradigm have revealed promising findings in relation to adolescents with and without chronic pain (Heathcote et al., 2015, 2016; Lau et al., 2019), only one published study exists using ambiguous scenarios to measure IB in adults with chronic pain (Chan et al., 2020). This study, found it was a promising methodology, especially considering it was the first study to demonstrate an interaction between AB and IB in research exploring combined cognitive biases in the field of pain. Indeed, a key strength of this paradigm is that it can be modified to include open-ended responses that do not constrain participants to a pre-set list of

interpretations as opposed to the other paradigms mentioned previously. This is important as using a pre-set list of interpretations may not necessarily reflect the participant's personal interpretation of the ambiguous scenario. Additionally, compared to single-words and images, ambiguous scenarios can be created and tailored to the population under study (Schoth & Liossi, 2016). However, it should be noted that ambiguous scenarios are infrequently matched in terms of readability, with certain scenarios being easier to understand, or indeed more ambiguous than others. Additionally, the lack of use of filler scenarios may inadvertently prime participants (e.g., toward pain words) resulting in response biases.

In sum, given the advantages of this paradigm, and that it is a direct measure of IB, a modified version of the ambiguous scenarios task was the method of choice to investigate IB's in the present research. The design and validation of the ambiguous scenarios task is presented in Chapter 4 and its use in Chapters 5 and 6.

2.4 Cognitive Paradigms Investigating Pain-related Memory Biases

The predominant method of assessing MB in chronic pain is via the use of free recall tasks. However, while free recall tasks are robust, there is evidence to suggest that recognition tasks are a more sensitive measure of MB. These paradigms will be discussed in turn below.

2.4.1 Free Recall Tasks

The most frequently used method to measure MB in adults with chronic pain is the free recall paradigm (for review see Schoth et al., 2020). This paradigm typically involves participants being presented with a list of words, some of which are pain/illness-related and some neutral (encoding stage). A distractor task (e.g., counting backwards from 999 in 3s for 2 minutes) is then sometimes used to clear any words that might be in a participant's short-term memory and prevent any new information transferring to long-term memory. Following this, participants are presented with a

free recall task, which requires them to recall as many words as possible from the previously presented word lists within a given time frame.

Pincus and Morley (2001) conducted a narrative review totalling 7 studies (5 with adults, 2 with children) examining whether individuals with pain display recall biases for pain and/or illness-related words. Of the five studies concerning adults, only two reported effect sizes regarding the recall of sensory-pain versus neutral words (0.33 – 0.78). In short, Pincus and Morley (2001) suggested that chronic pain patients display a recall bias for sensory-pain words, and that concurrently depressed pain patients (also included in the review) show a broader recall bias for health and illness-related words. This led to the authors concluding that there was 'robust' evidence for MB in chronic pain patients. However, these results do not accord with Schoth et al., (2020). Schoth et al. conducted a systematic review and meta-analysis of 12 studies exploring memory recall biases for pain-related information and concluding that the evidence for MB in patients with chronic pain was in fact 'inconclusive'. They reported no significant differences between chronic pain and pain-free controls in the recall of sensory-pain, illness-related or depression-related words. Thus, the evidence for recall bias in pain-research is currently mixed.

While free recall paradigms are argued to be the most reliable measure of recall biases, it is important to acknowledge that task instructions vary considerably among studies – which may be contributing factors to the heterogeneity of findings in this area. For instance, studies can employ explicit or surprise free recall tasks (e.g., Pincus et al., 1994; Schoth et al., 2015, 2016). Moreover, some choose to employ distractor tasks while others do not (e.g., Pauli & Alpers, 2002; Pearce et al., 1990), and the time allocated for recall can also differ (for review see Schoth et al., 2020). Other complicating factors including the mode of presentation (e.g., written, audio, computer) and that the completion of filler tasks (e.g., Stroop, visual-probe, word-generation) can also vary. Indeed, given that studies tend not to report the psychometric properties of their free recall paradigms, the reliability of these tasks are unknown. Schoth et al., (2020) further highlighted in their review that explicit and surprise recall tasks have not been directly compared in the field of chronic pain. Additionally, as arousing and highly valanced words are more likely to be recalled than neutral words, it is surprising that none of the studies included in the review

conducted by Schoth et al., (2020) obtained stimulus ratings for valence and arousal (Kensinger & Corkin, 2003). Hence, the main limitations of free recall paradigms appear to be associated with the variability in the heterogenous methodology of the studies that employ them.

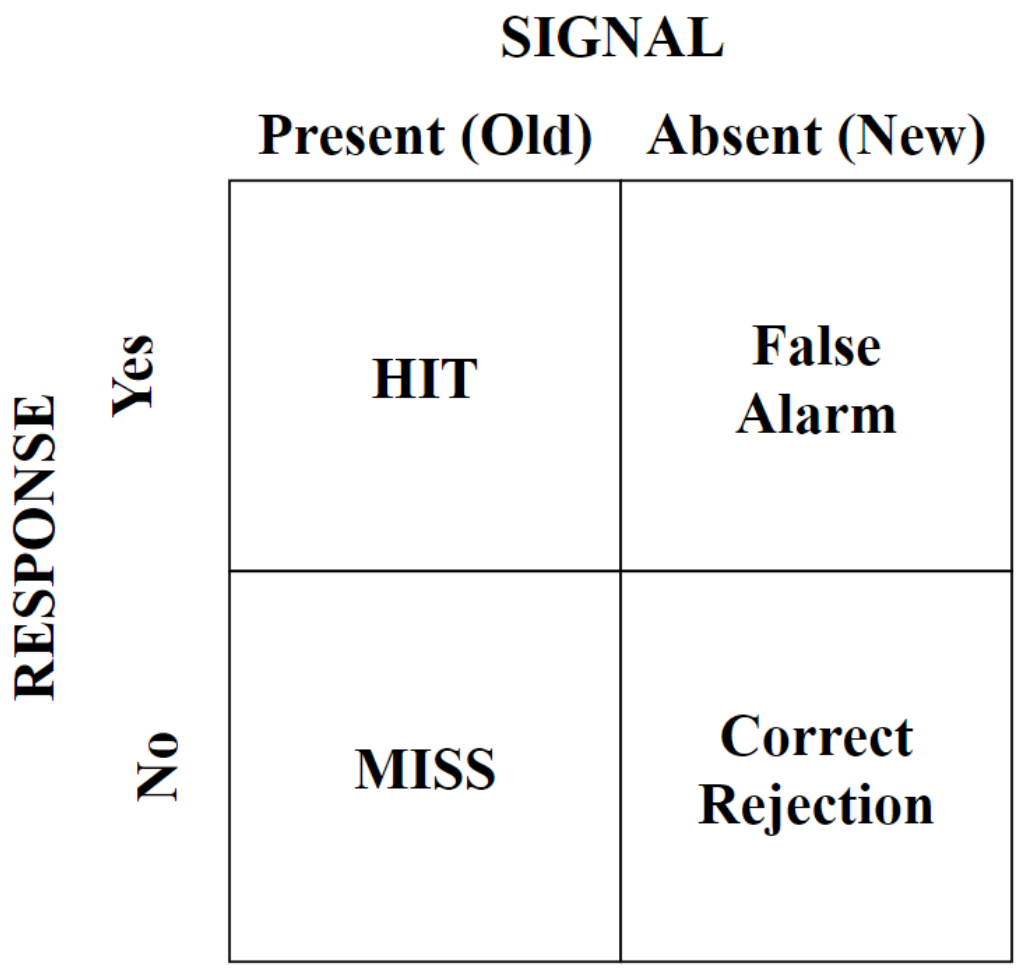
2.4.2 Recognition Tasks

It can be argued that recognition paradigms used to measure MB are more superior than the use of recall paradigms. While recall tasks require greater cognitive effort via self-initiated search and retrieval processes (Danckert & Craik, 2013), recognition tasks provide more efficient retrieval cues and involve comparison processes between the available and stored information. In recognition paradigms, participants are typically asked to report if a stimulus has been seen before (i.e., is 'old') or has not been seen before (i.e., is 'new').

Signal Detection Theory (SDT, Green & Swets 1966) is now a commonly employed method in recognition paradigms. Originating from the field of perception as a means of discriminating between signals (i.e., stimuli) and noise (i.e., no stimuli), this method has been applied in several areas of Psychology. Recognition biases are common in emotional memory studies (e.g., Buhlmann et al., 2006; Leppanen et al., 2004; Lundh & Ost, 1996), which often involve the presentation of stimuli (e.g., words/faces) and ask participants to make a choice whether the stimulus is old (i.e., it has been presented in a previous task) or new (i.e., it has not been presented in a previous task), which is commonly referred to as the 'Yes/No' recognition paradigm. SDT is useful here given that 'Old' stimuli represent 'signal' trials and 'new' stimuli represent 'noise' trials. One key benefit of adopting SDT is that rich data can be obtained while using the 'Yes/No' recognition paradigm. To expand, four categories of responses are generated depending on whether the participant answers 'Yes' or 'No' to an 'Old' or 'New' stimulus. For example, responding 'Yes' to an 'Old' stimulus is called a 'Hit', responding 'No' to an 'Old' stimulus is called a 'Miss', responding 'Yes' to a 'New' stimulus is called a 'False Alarm' and responding 'No' to a new stimulus is called a 'Correct Rejection' (see **Figure 2.7**). Importantly, this data also allows us to gain a measure of correct responses (by adding together the number of

'Hits' and 'Correct Rejections') and incorrect responses (by adding together the number of 'Misses' and 'False Alarms'), allowing researchers to gain a more detailed insight into the recognition biases displayed within their pain participant groups.

Figure 2.7: **Signal Detection Theory used in Psychology, where participants Yes or No answers to Old and New stimuli are sorted into one of four categories; hit (old – yes), miss (old – no), false alarm (new – yes), correct rejection (new – no).**



It is important to highlight that, to date, few studies within the field of pain have demonstrated how pain can bias memory – especially as free recall methodology is not able to provide concrete answers to such complex questions. To expand, classic recall tasks involve participants recalling the event, the stimulus and reporting what they can remember – which is all internal, with no external prompts. However, this paradigm cannot tell us what participants did not see in a precise way. Participants may mis-recall items and while an error-analysis is possible, with recognition paradigms such as the 'Yes/No' task allow for a more thorough explanation of these errors (through analysis of misses and false alarms). Indeed, Clark and Bennett-Clark (1993) assert that recognition memory provides the most sensitive means of determining the amount of information that has successfully entered one's long-term memory. This is a further limitation of free recall paradigms, which often are too close in time to the 'learning' phase (e.g., the same day; for review of free recall paradigms see Schoth et al., 2020) to allow true exploration of long-term memory biases.

Thus, a novel approach of using recognition tasks to assess MB in acute and chronic pain samples was utilised in the present thesis (Chapters 5 and 6). This approach was taken as it enables finer grained analysis of long-term memory biases at both short and long intervals.

2.5 Investigation of Cognitive Bias Summary

The present chapter, thus far, has described and evaluated the key experimental paradigms typically used to measure pain-related cognitive biases. Of these, the optimal measure of attentional bias is free viewing with eye tracking due to its ability to distinguish between the three main components of attention (engagement, disengagement, avoidance). With respect to IB, given its adaptability to the specific populations under study and potential to be modified to encourage open ended responses, the ambiguous scenarios task provides an optimal measure. Moreover, it avoids the pitfalls associated with constraining participants to pre-determined interpretations. Finally, with respect to MB, a novel approach to measuring MB using both free recall and recognition paradigms is preferential. This is because free recall allows for the measurement of

biases in more immediate memory and recognition allows for measurement of biases in delayed memory, enabling not only the investigation as to whether MB in pain changes over time but finer grained analysis of the effect of experimentally induced (i.e., acute) pain (Chapter 5) and chronic pain (Chapter 6) on long-term memory.

2.6 Pain Induction Methods in Humans

Pain induction methods in healthy participants are common given that they help to extend our understanding of the mechanisms of pain, assessment of pain, but also examine the psychological factors that accompany an acute pain experience (Edens & Gill, 1995). Indeed, it is currently unknown as to the temporal relationship of cognitive biases. For example, do these biases develop before or after one's pain becomes chronic? Considering this, experimental pain manipulations in healthy participants can provide valuable insight into the effects of acute pain on cognitive processes. Pain can be induced in the laboratory using mechanical, chemical, electrical, and thermal stimulation. These methods will be discussed and evaluated in turn below.

2.6.1 Mechanical Stimulation

Mechanical pain induction methods can be used to stimulate the skin, muscle, and viscera. Mechanical stimulation of the skin includes touch (i.e., via the application of pressure with a finger or Von-Frey hair), pinprick (i.e., stimulation of the skin via the use of a needle, safety pin or a thick Von-Frey filament) and pressure (i.e., stimulation via squeezing skin between two pressure sensors, or pinching a finger/toe/ear lobe between an algometer probe and a pinch handle).

While mechanical stimulation techniques have been used in some studies to induce pain (e.g., see van den Broeke & Mouraux, 2014; Kessler et al., 2006), it is important to note that each suffers from limitations. Mechanical stimulation of the skin using touch can apply an exact and reproducible pressure when using a Von-Frey hair, however, this method has been found to

activate low threshold mechanoreceptors and nociceptors. Hence, this method is not specific (Le Bars et al., 2001). The use of pressure has also been criticised on the same grounds as pinprick methods (Staahl & Drewes, 2004), for mechanically stimulating the skin and causing a decreased blood flow (i.e., local ischemia) which also induces pain (Reddy et al., 2012). Further, a shortcoming of using pinprick is that the speed of pain onset and offset is not able to be controlled easily. For these reasons, mechanical stimulation has been used infrequently in pain psychopathology.

2.6.2 Chemical Stimulation

Chemical methods of pain induction involve the use of chemical irritants, most notably capsaicin and mustard oil. These irritants are used to excite nociceptive nerve endings in humans via intracutaneous injection, topical application, or application to a blister base.

Capsaicin is an active ingredient that gives chilli peppers their hot taste and produces a burning sensation when applied to the skin of humans. This sensation can last for a long period of time (i.e., hours) after the removal of the cream. That said, a cooling agent (i.e., menthol) can be applied to the site where burning is occurring to relieve it. It is suggested that pain induced via capsaicin serves as a surrogate model of changes observed in neuropathic pain (Reddy et al., 2012). Mustard oil has predominantly been used to induce pain in rats (see Bonjardim, 2009; Jiang & Gebhart, 1998) and more recently humans (Andersen et al., 2017). Mustard oil induces pain via inflammation and thermal/mechanical hyperalgesia. A major limitation of these chemical methods, as already alluded to, is that their onset and time courses are variable (Handwerker & Kobal, 1993). As such, very few studies have used topical applications of these chemical substances to induce pain in humans.

2.6.3 Electrical Stimulation

Like mechanical and thermal methods, electrical stimulation can be applied to the skin, muscle and viscera. In relation to the skin, electrical stimulator devices are applied to the skin surface or intracutaneous tissue. The device can be modified to produce a different stimulation pattern including different waveforms, frequencies, and durations. A controlled current is then passed through the area of the skin where the stimulator device has been applied. Low-level electrical outputs are typically able to induce a moderate-to-strong pain sensation. However, this method of pain induction exhibits selectivity in the afferents and nervous structures activated and thus induces different kinds of pain (Reddy et al., 2012).

A strength of using electrical stimulation is that it can provide rapid stimulation and is easy to replicate (Edens & Gill, 1995). However, there are many limitations, for instance electrical methods excite afferent pathways and peripheral nerve fibres in an unnatural manner (Handwerker & Kobal, 1993). Further, electrical stimulation may be perceived as discomfort as opposed to pain (Edens & Gill, 1995). Lastly, electrical stimulation bypasses sensory nerve fibres activating the nerve fibres directly, this means that information pertaining to transduction is lost and the method is not a specific activation of nociceptors (Reddy et al., 2012).

2.6.4 Thermal Stimulation

Thermal stimulation methods include contact heat, radiant heat (i.e., laser), cold stimulation (i.e., cold-pressor pain) and burn injury. In relation to heat stimulation, a pelter thermode is typically used to cause heating. At threshold determinations, A-delta fibres are activated by rapid skin heating termed ‘first pain’, C-fibres are then activated causing ‘second pain’ that is often described as ‘throbbing, burning or swelling’. Ardent-Nielsen and Chen (2003) state that the high and low temperature limit should be between 50 degrees and 5 degrees to prevent any damage to the skin. Other methods of heat stimulation include laser stimulation (whereby laser pulses evoke a distinct pricking pain in the skin), focused light and burn injury. Heat stimulation methods have been

criticised, most notably, as contact heat stimulators cause mechanical activation of the skin and low-threshold non-nociceptors (Reddy et al., 2012). Thus, care is needed with regards to thermode-skin contact and pressure of application to ensure that pain is being induced in a standardised fashion. Indeed, the above is cited as a reason for the limited use of heat stimulation, given the technical issues surrounding the need to deliver rapid and repetitive heat energy to the skin (Granot et al., 2006).

Cold stimulation methods include the cold-pressor task, freeze legion, a cold gel bag, wet alcohol sponge, menthol or a felter thermode applied to the skin to induce a cold sensation (Staahl & Drewes, 2004). Although originally intended for use in studies on hypertension, cold stimulation via the cold-pressor task is arguably one of the most common pain induction methods used in acute experimental pain research. This method involves participants first placing their hand in warm water to control for initial wrist temperature. Next, participants place their hand up to the wrist into a cold-pressor tank at a temperature of 5 degrees for as long as possible (up to a maximum of 240 seconds). This method induces pain via the initial vasodilation of the blood vessels when the wrist is in the warm water, followed by vasoconstriction of the blood vessels when the wrist is in the cold water (Boston & Sharpe, 2005).

A limitation of this thermal pain induction method is that pain onset and offset is gradual. Moreover, studies vary considerably in both the equipment and methodology used (Birnie et al., 2014). For instance, studies differ in the temperature of circulating water and the maximum time participants submerge their wrist in the cold water. Indeed, Mitchell et al., (2004) provides evidence to suggest that minor changes in experimental protocol to the cold-pressor task can result in significant differences in pain intensity and tolerance. The Cold Pressor Task (CPT) has also been criticised as participants can potentially adapt to the numbing effects of the cold water. However, research suggests that the CPT possesses excellent 2-week test-retest reliability to assess pain threshold and pain intensity in non-clinical samples (e.g., Koenig et al., 2014). MacLachlan et al., (2016) also found that threshold measures obtained from the cold-pressor task are predictive of prolonged pain outcomes (MacLachlan et al., 2016). The most notable strength, however, is that the CPT is argued to mimic the effects of chronic pain conditions effectively because of its

unpleasantness (Woolf, 1979, cited in Mitchell et al., 2004; Dubin & Patapoutian, 2010). Moreover, C-fibres are argued to mediate cold-pain in humans to a greater extent, which produces secondary pain (i.e., dull, deep, throbbing) which is more consistent with acute/chronic pain (Staahl & Drewes, 2004). Considering this, the cold-pressor task was determined the most valid method to use when inducing experimental pain in Study 3 (Chapter 5).

2.6.5 Pain induction Methods Summary

The key techniques used to experimentally induce pain are electrical and thermal stimulation. Of these, the CPT is a preferential method to experimentally induce pain, given that it has been argued to be the closest method to replicating the effects of chronic pain conditions (Woolf, 1979, cited in Mitchell et al., 2004) and was therefore used to experimentally induce pain in this PhD research (Chapter 5).

Chapter 3 **Measuring Attentional Biases using Pain-related Pictorial Stimuli: A Stimulus-validation Study.**

3.1 Introduction

The literature regarding attentional bias (AB) and pain is marked by a large variability in findings. AB has been demonstrated in a variety of pain conditions, including musculoskeletal pain (Schoth et al., 2015), rheumatoid arthritis (Sharpe et al., 2009) and chronic headache (Schoth & Liossi, 2010). Yet, other studies employing the same populations have reported no such biases (e.g., Roelofs et al., 2003; Asmundson & Hadjistavropoulos, 2007).

Methodological inconsistencies between studies, including different stimulus types, may account for this variability (as highlighted in Chapter 2, section 2.1**)**. Dear et al. (2011) explored the importance of personal relevance and ecological validity of stimuli in a sample of chronic pain patients and matched pain-free controls. Using a dot-probe paradigm, they presented word and picture-based stimuli to detect ABs using generally selected (lower personal relevance) and idiosyncratically selected (higher personal relevance) stimuli. Results showed that both groups displayed an AB for idiosyncratically selected pictorial stimuli, but not for idiosyncratically or generally selected pain-related word stimuli. Hence, while AB can be observed in both clinical and non-clinical populations, stimulus-related factors may impact the ability to detect these biases.

Despite the above findings, pain-related word stimuli have typically been used to detect ABs in chronic pain (Deghani et al., 2003; Sharpe et al., 2009; Liossi et al., 2009; Haggman et al., 2010; Schoth et al., 2018, 2019). However, word stimuli lack ecological validity and require cognitive processing; hence they may be limited in initial threat (or pain) value (Schimmack, 2005). Thus, it is questionable whether word stimuli are sufficient to accurately measure pain-related ABs.

Importantly, the mixed findings observed in studies using pain-related word stimuli may be explained by the recently proposed Threat Interpretation Model (TIM, Todd et al., 2015; see Chapter 1, section 1.3.6). To recap, the TIM argues that for an AB to be observed stimuli must first be interpreted as threatening and possess a medium to high threat value for attentional processes to be influenced (i.e., vigilance or avoidance). Consequently, the pain-related word stimuli used in some prior studies may not be sufficiently threatening to capture the selective attention of chronic pain patients, resulting in normal attentional processing.

Pictorial stimuli are more ecologically valid than word stimuli (Dear et al., 2011). Yet, few stimulus databases that contain pain and/or injury-related pictorial stimuli exist. The most popular broad-topic databases with pain-related pictorial stimuli include the International Affective Picture System (IAPS, Lang et al., 1997; Lang & Bradley, 2007), the Geneva Affective Picture Database (GAPED, Dan-Glauser & Scherer, 2011) and the Psychological Image Collection at Stirling (PICS, pics.stir.ac.uk). The IAPS is a standardised database of colour images whereby normative ratings (i.e., pleasure, arousal, dominance) are provided for each stimulus. These images have been used extensively in emotion and attention research and are considered a 'gold standard' (Balsamo et al., 2020). Similarly, the GAPED is a colour picture database that consists of 730 pictures that focus on valence and normative significance. This database includes pictures designed to induce threat (e.g., Spiders/Snakes) and scenes related to human rights violations (e.g., skin burns to young children) and animal mistreatment. Positive (e.g., nature scenes) and neutral (e.g., inanimate objects) pictures are also included. Data pertaining to valence and arousal ratings are available for each picture. Lastly, the PICS provides a collection of images for use in psychology research, with a number of 2D stimulus sets, including faces of 10 men and 13 women, depicting painful and neutral facial expressions. No rating data currently exists for the PICS stimuli.

Of note, a key issue of these stimulus sets is that they are limited in stimuli specifically designed for investigating cognitive biases in pain. Moreover, there is variation in the emotional properties of the stimuli reported – for example, IAPS and GAPED report valence (i.e., how positive or negative a stimulus is) and arousal (i.e., how exciting a stimulus is), whereas the PICS does not. This is important, as theories of emotion processing postulate two opposing systems as

responsible for emotion processing; namely, the appetitive system and the defensive system (e.g., Motivational Priming Theory or MPT; Lang et al., 1995). Appetitive stimuli include those which reflect our intrinsic motivation to satisfy bodily needs (e.g., Food, Sex). Fulfilment of bodily needs facilitates positively valanced emotions (e.g., Happiness/Joy). In contrast, the defensive system is activated in the presence of aversive/threatening/harmful (noxious) stimuli contributing to negatively valanced emotions (e.g., Fear/Sadness/Disgust). Hence, measures of valence and arousal are important for pain-related pictorial stimuli, given that they can contribute to negative emotions which subsequently impact upon pain perception (Godinho et al., 2012; Rhudy et al., 2007). Previous research is consistent with the key tenets of MPT, finding that unpleasant affective states enhance pain perception, while pleasant affective states attenuate pain perception (Reicherts et al., 2013; Shaygan et al., 2017). This potentially makes it difficult to disentangle pain effects from unpleasant, or pleasant, affective states associated with the image. Indeed, to fully investigate pain biases in AB other emotional properties of pain-related stimuli are important. For example, threat value and pain intensity.

The TIM (Todd et al., 2015) makes key theoretical predictions regarding AB depending on the perceived threat level of a stimulus. Low threat is presumed to lead to easy disengagement of attention; moderate threat to more difficultly disengaging attention; and high threat to attentional avoidance. Given that previous research (e.g., Fashler & Katz, 2014, 2016) has demonstrated that adults with chronic pain display an AB to pain and/or injury-related images, obtaining measurements of threat for the stimuli presented would allow researchers to test the theoretical predictions of the TIM. For example, a stimulus set which has normative ratings for pictorial threat value would allow research to examine that prediction of the TIM; that is, whether attentional processes differ under varying levels of threat (low, medium, high). Moreover, it remains unclear in pain-related AB research as to whether the attentional processes observed reflect the pain aspects of these stimuli or their threat value more generally; as currently no pictorial stimulus set contains pain intensity rating (albeit ratings of threat, valence and arousal have been provided for 160 Chinese words, see Ho et al., 2015). Measurement of pain intensity is therefore of equal importance, to be able to gain a deeper understanding of how stimulus properties impact the processing of pain-related information in individuals with acute and/or chronic pain. This would,

consequently, allow current theories of pain (e.g., TIM) to be investigated (i.e., supported, or refuted).

Research has shown that emotions and pain are highly interconnected (Reicherts et al., 2013; Berna et al., 2010). For example, as alluded to previously, positive emotions (e.g., Happiness, Joy; Ruiz-Aranda et al., 2010; Kenntner et al., 2007) have been shown to reduce pain perception, whilst the opposite is true for negative emotions (Sadness, Fear; Bayet et al., 2014; Godinho et al., 2012; Meagher et al., 2001). However, research examining the impact of pain on emotion processing is lacking. That said, Godinho et al., (2008) recruited a sample of healthy participants and asked them to rate a series of affective images whilst receiving acute experimental pain (i.e., painful [or innocuous] electrical shocks). Findings showed a marked effect on pleasant pictures – such that, they were rated as significantly less pleasant; albeit no effects of acute experimental pain were found on the unpleasant images (i.e., they were not rated significantly more unpleasant). Nevertheless, these findings demonstrate that the experience of pain can influence subjective ratings of emotional images. Therefore, obtaining measurements of generalised anxiety/depression and recent pain experiences is important, given they could influence the normative ratings assigned to a stimulus.

Considering the above, the present study aimed to validate pain/injury-related and neutral stimuli taken from already existing broad-topic databases. These are the IAPS, GAPED and PICS. In the present study, the stimuli obtained from the above databases were validated to establish ratings of valence, arousal, pain intensity and threat value. Participants were also asked to complete the Recent Pain Experiences Questionnaire (adapted from Cleeland & Ryan, 1994) and the DASS-21 (Henry & Crawford, 2005) to ascertain whether recent experiences of pain and/or depression/anxiety/stress symptomology influenced stimulus ratings. It was hypothesised that clear differences in pain-intensity, threat value, valence and arousal would be observed for the pain/injury images versus the neutral images; such that pain-related images would have higher ratings of pain intensity, threat value, arousal, and possess a negative valence, compared to the neutral images.

3.2 Method

3.2.1 Participants

Participants were recruited via distribution of a study advertisement. This advert stated inclusion criteria of normal or corrected-to-normal vision and of age 18 or over; and resulted in recruitment of an opportunity sample of 65 participants from the University of Derby (comprising both students and staff). 1 participant was excluded from analysis due to incomplete data. Thus, the final sample compromised 64 participants, including 12 males (18.75%), 51 females (79.69%) and 1 who preferred not to declare their gender (1.56%). The age of participants ranged from 18 to 50 years (M = 21.22, SD = 5.19). Most participants were British (67.18%), with English cited as the first language for the majority (75%) of the total sample. 67.2% of participants reported no history of Anxiety and/or Depression.

Prospective power analysis using G*Power indicated that to achieve a medium effect size (.50) and acceptable power (i.e., 0.8; with alpha set at 0.05, one-tailed) for a repeated-measures design, the calculated sample size required was 27. This power analysis was conducted based on one repeated-measures factors (stimulus type, with three levels; GAPED, IAPS, PICS). For compensation of their time and commitment to the study, students received course credit. Students who did not wish to obtain course credit and staff, were entered into a prize draw to win a £20 Amazon Voucher. The study was approved by the Human Sciences Research Ethics Committee at the University of Derby. This ethical approval was for in-person data collection only, due to the graphic nature of some of the pain-related images.

3.2.2 Materials and Design

3.2.2.1 Visual Stimuli

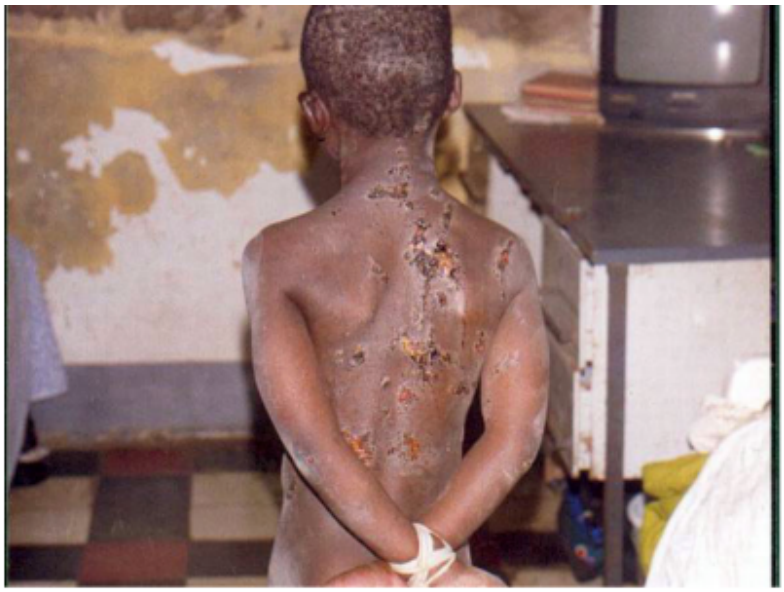
A total of 105 images were used as visual stimuli for validation. The pain stimuli consisted of forty-five pain images that were selected based on either of the two following criteria: i) the image(s) depicted pain and/or physical injury to a human (e.g., an image displaying an injured hand), or ii) the image(s) were facial expressions depicting pain. Of the 45 pain images, 25 satisfied criteria 1 (IAPS = 21, GAPED = 4), and 20 images satisfied criteria 2 (PICS). Whilst the aim was to maximise the number of available pain stimuli to be included for validation, GAPED pain-related images ***were not*** selected if they depicted pain and/or physical injury to a ***deceased*** human/animal.

The remaining 60 images were neutral (e.g., an image displaying a chair). Of the 60 neutral images, 22 were selected from the IAPS, 18 from the GAPED and 20 from the PICS. Neutral images were selected from the IAPS/GAPED if they depicted generic household objects, given these images possessed low levels of valence/arousal as provided in the available normative rating data by these databases. The 20 images from the PICS included the same 20 actors used in the pain facial expression images, but this time displayed a facial expression in a neutral pose. Following the selection of stimuli, the picture size of all IAPS and GAPED images was standardised to 640 x 480 pixels. Due to restrictions on the images obtained from the PICS, these stimuli could only be standardised to 640 x 512 pixels.

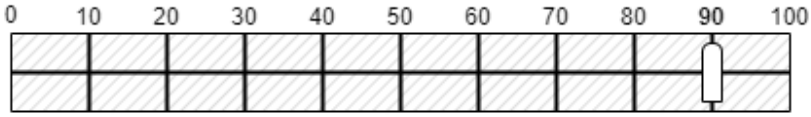
3.2.2.2 Validation Task

In the validation task participants were required to rate each image according to five different criteria (**see Figure 3.1**). These included pain intensity (i.e., how intense do you find the pain in the image presented?); threat value (i.e., how threatening do you find the image presented?); valence (i.e., how positive does the image look? ***and*** how negative does the image look?) and arousal (i.e., how strongly does this image make you feel? - adapted from research by Storbeck & Clore, 2008). Consistent with the methodology of Dan-Glauser and Scherer (2011) participants

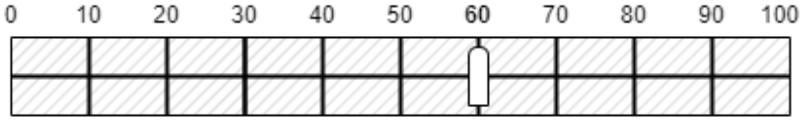
rated each image using a sliding scale ranging from 0 to 100 points (0 – not at all, 50 – mildly, 100 – very). Prior to the commencement of the task, participants were presented with 2 practice trials (using different stimuli) to familiarise themselves with the task requirements. Image presentation for the validation task was randomised throughout to avoid priming participants.



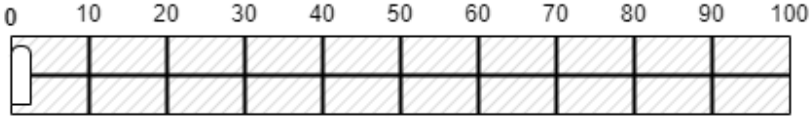
How intense do you find the pain in the image presented? (0 not at all, 50 mildly, 100 very).



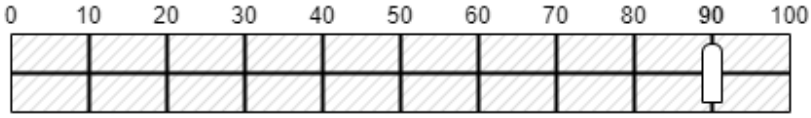
How threatening do you find the pain in the image presented? (0 not at all, 50 mildly, 100 very).



How positive does this image look? (0 not at all, 100 very positive).



How negative does this image look? (0 not at all, 100 very negative).



How strongly does this image make you feel? (0 not at all, 50 somewhat, 100 very).

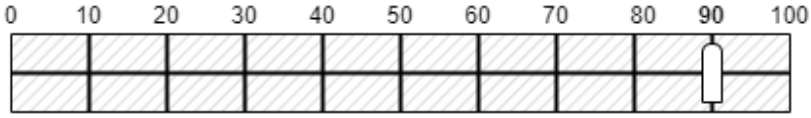


Figure 3.1: **Example Pain trial for rating according to five criteria; pain intensity, threat value, valence (positive, negative) and arousal.**

3.2.2.3 Questionnaires

Recent Pain Experiences Questionnaire (RPEQ)

To examine whether participant's subjective experiences of pain in the last three months influenced image stimulus ratings, four items derived from the Brief Pain Inventory Short-Form were used (adapted from Cleeland and Ryan, 1994). Consistent with Heathcote et al. (2016) and Said et al. (2019) participants were required to rate their: i) average pain intensity; ii) worst pain intensity in the past 3 months (0 = no pain, 10 = worst pain possible); iii) the amount that pain had interfered with daily activities over the past 3 months (0 = I don't miss out on any activities; 10 = I miss out on all activities) and iv); and the frequency of their pain over the last 3 months (1 = on less than 1 day each month, 10 = every day). The Brief Pain Inventory has been shown to be both reliable and valid across many cultures and languages (Cleeland & Ryan, 1994), and in the measurement of pain in numerous conditions including chronic non-malignant pain (Tan et al., 2004), osteoarthritis (Kapstad et al., 2010) and cancer pain (Kumar, 2011). Importantly, similar composite scores have been used in previous research measuring pain experiences in adult cancer patients (Ameringer, 2010) and aged populations (Parmelee et al., 1991).

Depression, Anxiety and Stress Scale (DASS-21)

To examine whether image stimulus ratings were influenced by depression, anxiety or stress the DASS-21 (Henry & Crawford, 2005) was used. The DASS-21 is a 21-item questionnaire, comprised of 3 sub-scales of 7 items each: depression, anxiety and stress. Participants are required to rate each item on a 4-point Likert-type scale ranging from 0 (does not apply to me at all) to 3 (applied to me very much, or most of the time). Initial sub-scale scores range from 0 to 21. Each score is then multiplied by 2 to calculate the final DASS-21 subscale score. Lower scores reflect normal functioning, and higher scores reflect extremely severe depression, anxiety and/or stress

respectively. Research has tested the psychometric properties of the DASS-21 and found each sub-scale possesses adequate internal consistency, concurrent validity and very good Cronbach's alpha values of .84, .74 and .79 for depression, anxiety and stress respectively (Antony et al., 1998; Musa et al., 2007; Asghari, et al., 2008; Wood, et al., 2010).

3.2.3 Procedure

Participants completed the experiment individually in a Psychology laboratory located in the University's Kedleston Road Campus. Qualtrics software was used to design the study. The entirety of the study was presented on a Lenovo T460 laptop (RAM = 8GH, 64-bit) with a screen size of 14 inches. Upon obtaining informed consent participants were presented with a brief demographic questionnaire. Following this, on-screen text outlined the instructions of the validation task. This required participants to rate each image (presented in random order) according to five different criteria in a standard order: pain intensity, threat value, valence (positive/negative) and arousal using a sliding scale from 0 – 100. Upon validation task completion, participants filled out the *RPEQ* and the *DASS-21* questionnaires. Next, to counter any potential negative effects of the stimuli utilised in the Validation Task on participants' mood, which is standard protocol in emotion research (Westerman et al., 1996), participants were required to select one of two videos taken from the online video-sharing platform YouTube. One video showed cats jumping and falling off various household objects, the second was a short clip of a well-known comedian's comedy roadshow. The clips were of a very similar duration and were selected for their humour. Once the video clip had ended, participants were then fully debriefed and thanked for their time. On average it took participants 45 minutes to complete the full study.

3.2.4 Data Screening

3.2.4.1 Participant Characteristics

As outlined in **Table 3.1**, on average participants reported mild levels of Depression and Anxiety and a moderate level of Stress (Lovibond & Lovibond, 1995). Additionally, participants reported low to moderate levels of pain in the preceding 3 months. There were no significant sex differences for any of these variables; depression U (12, 51) = 281.5, p = .667, two-tailed, anxiety U (12, 51) = 296.5, p = .868, two-tailed, stress U (12, 51) = 286, p = .725, two-tailed), recent pain experiences U (12, 51) = 262.5, p = .445, two-tailed).

Table 3.1: Means and SDs for the DASS-42 and Recent Pain Experiences Questionnaire.

QUESTIONNAIRE INDICES	MEAN (SD)
Depression (DASS-42)	11.96 (10.46)
Anxiety (DASS-42)	11.66 (9.64)
Stress (DASS-42)	15.60 (9.60)
Pain Frequency (last 3 months)	2.39 (1.36)
Pain Intensity (last 3 months)	2.53 (2.20)
Worst Pain Intensity (last 3 months)	5.05 (2.60)

Pain Interference (last 3 months)	2.08 (2.58)
Recent Pain Experiences (Composite)	12.14 (7.09)

3.3 Data Analysis

Due to incomplete data 1 participant was excluded, therefore, analyses were performed on the ratings of 64 participants. In the results section the mean rating and image outlier removal

procedure is presented first. Mean normative ratings for the pain and neutral images for each database are then compared, followed by a series of correlations between DASS-21 composite scores, RPEQ composite scores, and the normative ratings for the pain and neutral images. Finally, the images are separated into varying categories of pain intensity (i.e., neutral, low, and high) and threat value (low, medium, high) based on their mean pain intensity and threat value scores respectively.

3.4 Results

3.4.1 Mean Rating Calculations and Outlier Removal

Mean ratings were obtained for all stimuli from each of the three databases. All ratings ranged from 0 to 100. In accordance with previous research, the valence ratings were used as the criteria for identifying outliers (Dan-Glauser et al., 2011; McEwan et al., 2014). Images whose mean positive or negative valence rating exceeded the mean plus or minus two standard deviations were used as the criterion. That is, pain images for which the negative valence ratings were greater than the mean plus two standard deviations were removed. Similarly, pain images for which the positive valence ratings were lower than the mean minus two standard deviations were also removed. Neutral images for which the positive or negative valence were above or below the mean plus or minus two standard deviations were removed. However, no outliers were identified using this criterion and thus the stimulus set size remained at 105 images (**see Tables 3.2 – 3.3**).

Table 3.2: Valence outlier identification criteria (upper and lower acceptable values) for pain images (mean +/- 2 standard deviations)

Valence	Database	Lower Limit	Mean (SD)	Upper Limit
Positive	GAPED	-6.860	2.698 (4.779)	12.256
	IAPS	-5.548	3.248 (4.398)	12.044

	PICS	-17.919	4.325 (11.122)	26.569
Negative	GAPED	26.847	63.997 (18.575)	101.147
	IAPS	31.117	61.637 (15.260)	92.157
	PICS	1.884	29.266 (13.691)	56.648

Outlier definition was (a) Negative valence, score (outlier) > mean (pain images from given database) + 2SD; (b) Positive valence, score (outlier) < mean (pain images from given database) – 2SD.

Table 3.3: Valence outlier identification criteria (upper and lower acceptable values) for neutral images (mean +/- 2 standard deviations)

Valence	Database	Lower Limit	Mean (SD)	Upper Limit
Positive	GAPED	-28.825	15.065 (21.945)	58.955
	IAPS	-29.611	16.821 (23.216)	63.523
	PICS	-20.117	8.627 (14.372)	37.371
Negative	GAPED	-7.834	4.444 (6.139)	16.722
	IAPS	-8.195	3.695 (5.945)	15.585
	PICS	-6.339	11.367 (8.853)	29.073

Outlier definition was (a) Negative valence, score (outlier) > mean (pain images from given database) + 2SD; (b) Positive valence, score (outlier) < mean (pain images from given database) – 2SD.

3.4.2 Normative Rating Comparisons by Stimulus Type

A series of Bonferroni-corrected paired samples t-tests (using p <.01) were conducted to examine differences in mean normative ratings across pain intensity, threat value, positive valence, negative valence and arousal for the pain and neutral images taken from each database.

3.4.2.1 GAPED

Significant differences were observed across all normative ratings including; pain intensity t (64) = 26.771, $p < .001$, $d = 3.35$, *one tailed*, threat value t (64) = 10.611, $p < .001$, $d = 1.33$, *one tailed*, positive valence t (63) = - 4.684, $p < .001$, $d = -.59$, *one tailed*, negative valence t (64) = 24.285, $p < .001$, $d = 3.04$, *one tailed* and arousal t (64) = 17.350, $p < .001$, $d = 2.17$, *one tailed*. This was such that mean ratings of pain intensity, threat, negative valence and arousal were significantly higher for the GAPED pain images compared to the GAPED neutral images, except for positive valence of which the opposite was the case (see **Table 3.4**).

Table 3.4: Mean (SD) normative ratings for the pain and neutral images used from the GAPED.

	Pain Intensity	Threat Value	Positive Valence	Negative Valence	Arousal
Pain	59.29 (17.17)	30.99 (21.25)	2.70 (4.78)	63.99 (18.57)	48.87 (20.95)
Neutral	1.29 (3.40)	2.63 (4.26)	15.10 (22.12)	4.44 (6.14)	4.35 (6.66)

3.4.2.2 IAPS

Significant differences were observed across all normative ratings including; pain intensity t (64) = 32.707, $p < .001$, $d = 4.08$, *one tailed*, threat value t (64) = 15.360, $p < .001$, $d = 1.92$, *one tailed*, positive valence (t (64) = - 4.968, $p < .001$, $d = -.62$, *one tailed*, negative valence t (64) = 29.572, $p < .001$, $d = .3.70$, *one tailed* and arousal t (64) = 20.893, $p < .001$, $d = 2.61$, *one tailed*. This was such that mean ratings of pain intensity, threat, negative valence and arousal were significantly higher for the IAPS pain images compared to the IAPS neutral images, except for positive valence of which the opposite was the case (see **Table 3.5**).

Table 3.5: Mean (SD) normative ratings for the pain and neutral images used from the IAPS.

	Pain Intensity	Threat Value	Positive Valence	Negative Valence	Arousal
Pain	63.40 (15.29)	39.12 (19.39)	3.25 (4.40)	61.64 (15.26)	48.83 (18.15)
Neutral	1.53 (3.79)	2.49 (4.26)	16.82 (23.22)	3.70 (5.95)	4.23 (6.63)

3.4.2.3 PICS

Significant differences were observed across all normative ratings including; pain intensity t (64) = 13.553, $p < .001$, $d = 1.69$, *one tailed*, threat value t (64) = 1.775, $p = .04$, $d = .22$, *one tailed*, positive valence t (63) = - 5.263, $p < .001$, $d = -.66$, *one tailed*, negative valence t (64) = 11.764, $p < .001$, $d = 1.47$, *one tailed* and arousal t (64) = 8.236, $p < .001$, $d = 1.03$, *one tailed*. This was such that mean ratings of pain intensity, threat, negative valence, and arousal were significantly higher for the PICS pain expression images compared to the PICS neutral expression images, except for positive valence of which the opposite was the case (see **Table 3.6**).

Table 3.6: Mean (SD) normative ratings for the pain and neutral facial expression images used from the PICS.

	Pain Intensity	Threat Value	Positive Valence	Negative Valence	Arousal
Pain	28.83 (16.27)	9.34 (9.75)	4.33 (11.12)	29.27 (13.69)	13.63 (10.00)
Neutral	3.10 (3.97)	7.15 (7.94)	8.62 (14.37)	11.37 (8.85)	5.80 (7.10)

3.4.3 Developing New Stimulus Categories

3.4.3.1 Pain Intensity

To distinguish between neutral, low, and high pain intensity images, the upper and lower quartiles of the mean ratings for all stimuli were calculated. This was calculated by identifying the mean pain intensity rating for all 105 images, calculating the Interquartile Range (IQR), and then computing where the 25^{th} and 75^{th} percentiles lay. This identified the threshold for the lower quartile as ratings that fell below 2.761, and for the upper quartile ratings that were above 40.231. Stimuli that fell within the lower (scores ranging from 0 – 2.761, with the highest score in this category being 2.5), middle (scores ranging from 2.762 to 40.231, with actual scores ranging from 3.28 – 40.31) and upper quartile (scores ranging from 40.232 – 100, with actual scores ranging from 41.72 – 91.25) were categorised as 'Neutral', 'Low Pain Intensity' and 'High Pain Intensity', respectively. All stimuli fell within these parameters, including 47 'Neutral', 35 'Low Pain Intensity' and 23 'High Pain Intensity' images. Means and Standard Deviations for the images included in each Pain Intensity category are displayed in **Table 3.7** below.

Table 3.7: Mean Pain Intensity (SD) for the images included in the neutral, low pain and high pain categories.

Pain Intensity Category	Mean (SD)
Neutral	1.068 (.738)
Low Pain Intensity	20.43 (13.97)
High Pain Intensity	65.08 (3.07)

As expected, all images in the 'neutral' category (n = 47) were originally described as 'Neutral' in their original database classifications (i.e., IAPS, GAPED, PICS) and all images in the 'High Pain Intensity' category (n = 23) were originally classified as pain related in their original database classifications. However, of the 35 images in the 'Low Pain Intensity' category, 22 were categorised as 'pain stimuli' and 13 as 'neutral' according to their original database classifications by the IAPS/GAPED/SPFD. In other words, 13 neutral stimuli achieved a Pain Intensity rating that would result in them being included in the low-pain intensity category. Consequently, these 13 neutral stimuli were removed. The number of final stimuli in each category is outlined in **Table 3.8** below:

Table 3.8: Number of remaining stimuli included in the neutral, low pain and high pain categories.

Stimulus Type	Neutral	Low Pain Intensity	High Pain Intensity
Non-Face Image	35	3	22
Face Image	12	19	1
Total	47	22	23

Following this, a one-way between-groups ANOVA was conducted to compare pain intensity ratings across the three groups (neutral, low pain intensity, high pain intensity). As data violated Levene's test for homogeneity of variance, statistics are reported from the Welch test.

There was a statistically significant difference at the $p < .001$ level in pain intensity scores for the three groups $F(2, 28.78) = 319.25$, $p < .001$, $\eta^2 = .91$. Bonferroni corrected post-hoc comparisons indicated that the mean pain intensity score for the neutral images, was significantly lower than the mean pain intensity score for the low pain images and also the high pain intensity images ($p < .01$ in both cases). Additionally, the mean pain intensity score for the low pain images was significantly lower than the mean pain intensity score for the high pain images ($p < .001$).

3.4.3.2 Threat Value

To distinguish between low, medium, and high threat images, the upper and lower quartiles of the mean ratings for all stimuli were calculated. This was calculated by identifying the mean threat value for all 105 images, then calculating the Interquartile Range (IQR), and then computing where the 25th and 75th percentiles lay. This identified the threshold for the lower quartile as ratings that fell below 6.477, and for the upper quartile ratings that were above 19.687. Stimuli that fell within the lower (scores ranging from 0 – 6.477, with the highest score in this category being 6.36), middle (scores ranging from 6.478 to 19.687, with actual scores ranging from 6.61 – 19.02) and upper quartile (scores ranging from 19.688 – 100, with actual scores ranging from 19.80 – 33.71) were categorised as 'Low Threat', 'Medium Threat and 'High Threat' respectively. All stimuli fell within these parameters, including 24 'Low Threat', 54 'Medium Threat and 27 'High Threat' images. Means and Standard Deviations for the images included in each threat category are displayed in **Table 3.9** below.

Table 3.9: Mean Pain Intensity (SD) for the images included in the neutral, low pain and high pain categories.

Threat Value Category	Mean (SD)
Low Threat	4.16 (1.66)
Medium Threat	11.68 (3.63)
High Threat	28.53 (.75)

All images in the 'Low Threat' category (n = 24) were originally described as 'Neutral' by their original database classifications (i.e., IAPS, GAPED, PICS). Of the images in the 'Medium Threat' category (n = 54), 33 were originally categorised as 'Neutral' and 21 as 'Pain' in their original databases. Of the stimuli included in the High Threat category (n = 27), 24 stimuli were originally assigned the label of 'Pain' and 3 'Neutral'. Given that 'Neutral' stimuli are not designed to possess a High Threat value, these 3 stimuli were removed. The number of remaining stimuli in each category is outlined in **Table 3.10** below.

Table 3.10: Number of remaining stimuli included in the low, medium and high threat categories.

Stimulus Type	Low Threat	Medium Threat	High Threat
Non-Face Image	21 (Neutral)	20 (19 Neutral, 1 Pain)	24 (Pain)
Face Image	3 (Neutral)	34 (14 Neutral, 20 Pain)	0 (Pain)
Total	24	54	24

A one-way between-groups ANOVA was conducted to compare threat ratings across the three groups (low threat, medium threat, and high threat). As data violated Levene's test for homogeneity of variance, statistics are reported from the Welch test. There was a statistically significant difference at the $p < .001$ level in threat value for the three groups $F(2, 104) = 367.411$, $p < .001$, $\eta^2 = .88$. Bonferroni corrected post-hoc comparisons indicated that the mean threat value for the low threat group was significantly lower ($p < .001$) than the mean threat value for the medium threat group. Additionally, the mean threat value for the high threat group was significantly higher than the mean threat value for both the low threat ($p < .001$) and medium threat groups ($p < .001$).

3.4.4 Final Stimulus Sets

3.4.4.1 Mean Normative Ratings for all Images

The full stimulus set comprising all the 105 images with mean ratings of Pain Intensity, Threat Value, Negative Valence, Positive Valence, and Arousal are displayed in **Table 3.11** below.

Table 3.11: Mean (SD) Normative Ratings (Pain Intensity, Threat Value, Valence, Arousal) for all Images included for Validation, and their respectively assigned Pain Intensity and Threat Value Categories.

Image ID	*Stimulus Category*	*Mean Pain Intensity*	*SD*	*Mean Threat Value*	*SD*	*Mean Valence Positive*	*SD*	*Mean Valence Negative*	*SD*	*Mean Arousal*	*SD*	*Pain Intensity Stimulus Set*	*Threat Value Stimulus Set*
GAPED HO38	Pain	72.34	23.01	40.94	32.11	.00	.00	78.75	22.57	61.88	28.27	High	High
GAPED H064	Pain	67.50	21.31	45.47	32.51	.95	3.46	70.31	24.81	52.97	26.76	High	High
GAPED H083	Pain	61.43	23.20	23.17	28.27	6.77	14.69	66.19	26.24	57.46	21.28	High	High
IAPS 2717	Pain	41.72	26.40	40.78	30.36	1.59	5.15	56.09	30.22	43.44	27.63	High	High
IAPS 3030	Pain	82.81	20.19	49.69	32.27	.79	3.73	79.53	21.63	63.75	27.02	High	High
IAPS 3103	Pain	76.25	20.74	38.91	29.45	.63	3.02	72.50	22.04	56.72	23.90	High	High
IAPS 3150	Pain	91.25	16.57	60.94	29.85	.00	.00	88.28	19.24	75.47	29.70	High	High
IAPS 3160	Pain	58.44	25.21	27.97	27.67	2.06	8.64	58.13	25.87	44.38	28.70	High	High
IAPS 3180	Pain	53.44	24.38	32.50	27.08	1.59	4.82	64.06	23.42	46.25	28.47	High	High
IAPS 3181	Pain	72.66	22.55	43.75	28.70	1.11	4.79	73.44	24.64	52.66	28.18	High	High
IAPS 3185	Pain	61.41	25.44	32.70	27.01	1.45	5.39	60.63	26.78	41.11	29.67	High	High
IAPS 3191	Pain	65.94	25.80	51.88	33.71	.95	3.46	72.81	28.09	58.44	29.02	High	High
IAPS 3195	Pain	69.53	23.26	41.56	31.18	1.11	3.64	65.63	26.60	50.78	31.41	High	High

IAPS 3211	Pain	47.97	29.72	29.22	29.72	13.33	18.05	39.06	28.21	37.03	27.79	High	High
IAPS 3213	Pain	86.09	16.96	50.00	32.56	3.65	12.99	78.59	23.76	69.22	24.44	High	High
IAPS 3215	Pain	58.28	20.82	25.63	24.68	2.54	7.61	58.28	25.30	41.09	22.75	High	High
IAPS 8230	Pain	71.25	24.66	46.25	29.89	1.43	4.70	63.75	26.87	41.09	30.41	High	High
IAPS 9042	Pain	73.59	23.12	44.53	33.14	1.90	7.15	63.91	29.85	57.34	25.97	High	High
IAPS 9402	Pain	90.00	18.26	58.13	30.28	1.75	12.64	86.88	21.52	72.81	25.39	High	High
IAPS 9582	Pain	42.50	24.62	23.75	23.80	7.62	14.11	37.66	23.14	30.00	29.68	High	High
IAPS 9590	Pain	49.06	25.93	38.13	29.65	4.13	11.02	46.09	27.75	41.25	30.44	High	High
IAPS 9599	Pain	59.53	25.04	35.63	27.13	4.06	9.71	55.31	24.81	41.25	15.93	High	High
PICS M9P10	Pain	43.75	24.33	13.28	15.33	3.02	12.78	40.16	23.20	18.91	14.33	High	Medium
GAPED H095	Pain	36.56	20.18	14.69	19.02	3.17	8.58	41.56	22.83	23.91	29.40	Low	Medium
IAPS 3280	Pain	39.53	22.99	20.31	22.61	10.16	16.90	34.06	23.55	24.84	28.29	Low	High
IAPS 9592	Pain	40.31	28.51	29.69	32.80	5.87	11.45	39.69	31.62	36.88	27.80	Low	High
PICS F1P6	Pain	29.22	21.70	7.30	10.19	3.49	13.46	31.09	23.24	15.47	13.90	Low	Medium
PICS F2P4	Pain	17.34	17.57	8.57	13.42	3.17	10.45	22.34	18.06	10.63	10.96	Low	Medium
PICS F5P4	Pain	16.56	14.50	12.66	17.30	4.60	15.54	23.28	16.43	8.59	13.22	Low	Medium
PICS F4P1	Pain	32.81	20.58	6.41	9.66	2.86	10.69	31.25	17.04	13.28	14.50	Low	Medium

PICS F6P7	Pain	25.00	20.16	9.37	14.35	3.49	13.22	31.25	21.42	13.44	13.73	Low	Medium
PICS F7P8	Pain	31.09	19.77	7.66	11.92	3.17	13.05	29.84	19.48	13.59	18.49	Low	Medium
PICS F9P7	Pain	36.72	21.90	7.81	13.15	2.70	10.35	36.56	22.76	19.06	17.48	Low	Medium
PICS F10P2	Pain	37.78	21.51	12.06	16.48	1.94	9.38	35.71	21.83	19.05	12.53	Low	Medium
PICS F11P2	Pain	20.16	17.77	5.16	10.39	3.17	9.47	21.72	18.73	9.84	10.98	Low	Medium
PICS F13P6	Pain	21.25	17.77	4.06	8.30	6.03	18.45	20.16	16.76	9.69	21.98	Low	Medium
PICS M1P1	Pain	40.31	23.16	14.84	17.46	1.43	4.70	41.41	25.00	22.66	14.88	Low	Medium
PICS M2P9	Pain	37.50	22.54	9.21	13.71	4.76	15.33	33.91	21.05	14.06	13.93	Low	Medium
PICS M3P9	Pain	9.69	11.54	11.41	16.80	4.92	15.44	21.41	20.92	8.91	13.55	Low	Medium
PICS M4P8	Pain	27.19	27.05	8.28	12.67	10.32	20.87	22.66	20.57	11.88	17.00	Low	Medium
PICS M5P1	Pain	36.72	26.79	9.06	14.98	9.05	22.70	32.03	23.45	15.16	14.85	Low	Medium
PICS M6P2	Pain	28.44	22.34	12.97	17.25	4.44	12.92	27.66	20.91	12.81	8.59	Low	Medium
PICS M7P5	Pain	18.28	14.97	5.16	9.76	5.24	14.80	19.38	15.42	6.56	16.84	Low	Medium
PICS M8P8	Pain	32.34	22.66	12.34	16.59	4.92	16.15	31.72	22.44	16.41	19.03	Low	Medium
PICS M10P1	Pain	35.00	22.96	9.38	14.35	3.81	13.25	32.34	21.95	12.97	7.45	Low	Medium
GAPED N097	Neutral	4.22	16.02	2.19	6.78	25.56	31.36	4.84	12.34	9.53	11.39	Low	Medium
IAPS 7012	Neutral	6.25	17.77	9.22	15.15	8.57	19.25	7.97	14.82	8.59	15.74	Low	Medium

IAPS 7016	Neutral	5.16	12.47	7.50	15.43	10.16	21.06	7.34	15.25	7.50	9.02	Low	Medium
IAPS 7030	Neutral	5.00	15.33	10.00	18.34	10.00	22.43	11.09	18.35	6.72	5.45	Low	Medium
IAPS 7052	Neutral	3.28	9.60	1.25	4.18	23.81	31.18	2.03	7.17	5.00	11.11	Low	Low
PICS F2N1	Neutral	3.59	7.21	2.03	5.10	8.57	20.31	9.84	10.31	5.31	8.16	Low	Low
PICS F6N1	Neutral	8.44	12.24	5.78	13.89	4.92	11.62	13.28	14.70	6.25	7.50	Low	Medium
PICS F9N1	Neutral	3.91	8.28	4.13	8.91	9.37	19.83	9.22	12.76	5.63	8.49	Low	Medium
PICS F10N1	Neutral	3.44	7.81	2.34	6.36	13.65	22.38	7.50	11.82	4.06	9.92	Low	Low
PICS F13N1	Neutral	3.28	8.92	5.00	8.73	4.92	15.01	13.28	16.72	3.75	15.22	Low	Medium
PICS M1N2	Neutral	7.97	12.87	13.75	19.80	4.13	14.88	18.44	17.39	10.00	9.43	Low	Medium
PICS M3N1	Neutral	4.13	9.78	16.25	20.51	8.89	19.85	17.66	19.42	9.38	9.25	Low	Medium
PICS M9N1	Neutral	6.41	14.95	23.13	23.63	3.81	13.00	23.28	21.31	14.22	7.53	Low	Medium
GAPED N009	Neutral	1.75	7.73	1.59	7.00	16.88	27.36	2.22	9.24	2.19	10.67	Neutral	Medium
GAPED N014	Neutral	2.10	9.60	2.58	9.40	12.22	24.79	3.75	11.62	3.65	11.55	Neutral	Medium
GAPED N017	Neutral	.48	2.15	.95	2.96	24.06	28.93	2.70	8.46	6.72	6.19	Neutral	Low
GAPED N020	Neutral	.48	2.15	3.02	7.10	11.59	22.16	3.28	8.74	3.28	12.18	Neutral	Medium
GAPED N027	Neutral	1.27	5.82	2.22	7.28	20.79	30.12	4.69	11.95	5.94	6.67	Neutral	Medium
GAPED N035	Neutral	.47	2.78	1.56	5.11	12.70	23.91	3.13	8.33	2.50	5.27	Neutral	Low

GAPED N041	Neutral	.63	3.93	2.34	5.84	12.86	22.61	2.03	5.68	2.34	10.82	Neutral	Low
GAPED N046	Neutral	.47	2.13	4.38	10.97	12.70	25.54	3.44	9.63	4.38	7.66	Neutral	Medium
GAPED N061	Neutral	1.43	9.13	1.88	6.14	10.16	23.33	2.97	9.54	2.19	9.59	Neutral	Low
GAPED N079	Neutral	1.09	4.75	2.54	7.40	16.03	27.74	5.47	10.68	4.69	13.24	Neutral	Medium
GAPED N085	Neutral	2.50	9.59	5.94	11.91	12.38	21.38	9.22	17.76	6.56	11.48	Neutral	Medium
GAPED N089	Neutral	1.27	6.35	3.97	9.25	15.47	28.62	2.86	8.69	4.92	9.74	Neutral	Medium
GAPED N019	Neutral	.79	3.73	2.34	6.61	12.06	25.28	7.50	14.58	4.38	6.71	Neutral	Medium
GAPED N092	Neutral	.32	2.52	2.38	7.34	7.78	22.75	4.69	9.75	2.03	16.47	Neutral	Medium
GAPED N098	Neutral	.48	2.80	2.38	8.17	19.05	30.31	5.16	10.69	5.63	6.78	Neutral	Medium
GAPED N106	Neutral	.16	1.26	1.11	3.64	11.90	24.49	3.91	11.36	2.19	10.69	Neutral	Low
GAPED N107	Neutral	1.11	5.12	1.90	5.35	17.46	26.27	7.50	12.47	5.16	14.03	Neutral	Low
IAPS 7001	Neutral	.48	2.80	.63	3.04	22.19	33.69	1.43	6.69	4.69	8.10	Neutral	Low
IAPS 7002	Neutral	.16	1.26	1.25	4.18	19.05	31.04	1.41	5.00	2.97	9.41	Neutral	Low
IAPS 7003	Neutral	.00	.00	.48	2.15	15.78	26.54	.95	6.40	3.13	9.32	Neutral	Low
IAPS 7004	Neutral	.16	1.26	.16	1.26	20.94	31.15	.48	2.80	3.59	5.88	Neutral	Low
IAPS 7006	Neutral	.63	2.46	1.29	5.58	10.95	25.57	4.38	9.57	1.88	8.77	Neutral	Low
IAPS 7009	Neutral	.63	3.02	1.27	4.92	20.16	30.21	2.38	7.77	3.44	16.12	Neutral	Low

IAPS 7021	Neutral	2.03	5.96	2.50	8.16	16.03	27.68	5.31	12.97	3.91	13.81	Neutral	Medium
IAPS 7032	Neutral	.95	3.46	1.45	5.39	14.52	25.52	4.29	8.56	2.70	11.20	Neutral	Low
IAPS 7035	Neutral	.63	3.02	.47	2.13	17.62	28.94	3.28	10.09	3.75	5.48	Neutral	Low
IAPS 7041	Neutral	.94	4.62	.94	5.26	18.57	29.61	3.75	10.47	2.19	11.81	Neutral	Low
IAPS 7050	Neutral	1.43	6.92	4.29	13.04	14.92	27.87	3.91	13.87	4.69	11.13	Neutral	Medium
IAPS 7057	Neutral	.31	1.75	.78	4.10	26.51	32.29	2.81	9.17	5.63	7.06	Neutral	Low
IAPS 7080	Neutral	1.41	6.87	3.49	10.03	11.27	22.18	4.06	11.23	2.97	12.71	Neutral	Medium
IAPS 7081	Neutral	.32	1.77	.79	3.26	22.03	29.72	1.43	4.35	6.88	7.06	Neutral	Low
IAPS 7150	Neutral	1.11	6.50	2.81	9.51	16.67	28.90	4.38	10.06	2.97	8.10	Neutral	Medium
IAPS 7175	Neutral	.31	1.75	.63	3.02	16.83	28.39	2.34	7.92	2.97	8.83	Neutral	Low
IAPS 7211	Neutral	.48	2.15	1.75	4.93	15.94	30.43	2.06	7.22	3.49	8.74	Neutral	Low
IAPS 7950	Neutral	.63	3.02	.00	.00	18.13	28.67	2.86	10.54	3.28	9.22	Neutral	Low
PICS F1N1	Neutral	1.56	5.11	2.70	6.01	9.52	18.27	7.66	10.50	4.22	9.25	Neutral	Low
PICS F4N1	Neutral	1.75	4.59	3.81	7.50	10.48	18.68	7.62	10.88	4.13	11.30	Neutral	Medium
PICS F5N1	Neutral	2.34	5.56	11.88	16.12	5.71	12.79	15.16	17.27	7.34	9.34	Neutral	Medium
PICS F7N1	Neutral	1.25	3.78	3.28	7.36	16.51	24.37	5.31	9.92	4.06	10.52	Neutral	Medium
PICS F11N2	Neutral	2.50	6.42	3.44	8.21	7.46	17.22	13.13	14.68	5.31	7.01	Neutral	Medium

PICS M2N1	Neutral	1.41	5.87	7.78	11.28	8.57	22.06	8.13	11.25	5.16	13.79	Neutral	Medium
PICS M4N1	Neutral	.31	1.75	7.97	15.14	11.27	23.45	9.53	13.15	4.69	7.53	Neutral	Medium
PICS M5N1	Neutral	2.34	5.27	6.25	10.31	7.62	21.23	12.97	13.30	4.38	8.26	Neutral	Medium
PICS M6N1	Neutral	2.03	5.40	4.53	10.22	9.21	16.88	6.88	10.97	3.75	10.76	Neutral	Medium
PICS M7N1	Neutral	2.03	4.77	8.73	14.31	7.94	19.27	10.16	12.15	6.25	9.36	Neutral	Medium
PICS M8N2	Neutral	.78	3.24	2.38	6.65	14.29	22.48	4.38	9.74	3.91	18.15	Neutral	Medium
PICS M10N1	Neutral	2.50	5.91	7.03	10.19	5.87	16.81	14.06	13.77	4.38	28.27	Neutral	Medium

3.4.4.2 Pain Intensity

The full stimulus set comprising images split into 'Neutral', 'Low Pain Intensity' and 'High Pain Intensity' are displayed in Table 3.12 below. Of the 92 images displayed in Table 3.12 below, 47 fell into the Neutral category, 22 fell into the Low Pain Intensity category and 23 fell into the High Pain Intensity category.

Table 3.12: Images by Pain Intensity Category with Means.

IMAGE NAME	*Stimulus Category*	*Mean Pain Intensity Rating*	*Pain Intensity Category*
IAPS 7003	Neutral	0	Neutral
GAPED N106	Neutral	0.16	Neutral
IAPS 7002	Neutral	0.16	Neutral
IAPS 7004	Neutral	0.16	Neutral
IAPS 7057	Neutral	0.31	Neutral
IAPS 7175	Neutral	0.31	Neutral
PICS M4N1	Neutral	0.31	Neutral
GAPED N092	Neutral	0.32	Neutral
IAPS 7081	Neutral	0.32	Neutral
GAPED N035	Neutral	0.47	Neutral
GAPED N046	Neutral	0.47	Neutral
GAPED N017	Neutral	0.48	Neutral
GAPED N020	Neutral	0.48	Neutral
GAPED N098	Neutral	0.48	Neutral
IAPS 7001	Neutral	0.48	Neutral
IAPS 7211	Neutral	0.48	Neutral
GAPED N041	Neutral	0.63	Neutral
IAPS 7006	Neutral	0.63	Neutral
IAPS 7009	Neutral	0.63	Neutral
IAPS 7035	Neutral	0.63	Neutral
IAPS 7950	Neutral	0.63	Neutral
PICS M8N2	Neutral	0.78	Neutral
GAPED N019	Neutral	0.79	Neutral
IAPS 7041	Neutral	0.94	Neutral
IAPS 7032	Neutral	0.95	Neutral
GAPED N079	Neutral	1.09	Neutral
GAPED N107	Neutral	1.11	Neutral
IAPS 7150	Neutral	1.11	Neutral
PICS F7N1	Neutral	1.25	Neutral
GAPED N027	Neutral	1.27	Neutral
GAPED N089	Neutral	1.27	Neutral
IAPS 7080	Neutral	1.41	Neutral
PICS M2N1	Neutral	1.41	Neutral
GAPED N061	Neutral	1.43	Neutral
IAPS 7050	Neutral	1.43	Neutral
PICS F1N1	Neutral	1.56	Neutral
GAPED N009	Neutral	1.75	Neutral
PICS F4N1	Neutral	1.75	Neutral
IAPS 7021	Neutral	2.03	Neutral

PICS M6N1	Neutral	2.03	Neutral
PICS M7N1	Neutral	2.03	Neutral
GAPED N014	Neutral	2.1	Neutral
PICS F5N1	Neutral	2.34	Neutral
PICS M5N1	Neutral	2.34	Neutral
GAPED N085	Neutral	2.5	Neutral
PICS F11N2	Neutral	2.5	Neutral
PICS M10N1	Neutral	2.5	Neutral
PICS M3P9	Pain	9.69	Low
PICS F5P4	Pain	16.56	Low
PICS F2P4	Pain	17.34	Low
PICS M7P5	Pain	18.28	Low
PICS F11P2	Pain	20.16	Low
PICS F13P6	Pain	21.25	Low
PICS F6P7	Pain	25	Low
PICS M4P8	Pain	27.19	Low
PICS M6P2	Pain	28.44	Low
PICS F1P6	Pain	29.22	Low
PICS F7P8	Pain	31.09	Low
PICS M8P8	Pain	32.34	Low
PICS F4P1	Pain	32.81	Low
PICS M10P1	Pain	35	Low
GAPED H095	Pain	36.56	Low
PICS F9P7	Pain	36.72	Low
PICS M5P1	Pain	36.72	Low
PICS M2P9	Pain	37.5	Low
PICS F10P2	Pain	37.78	Low
IAPS 3280	Pain	39.53	Low
IAPS 9592	Pain	40.31	Low
PICS M1P1	Pain	40.31	Low
IAPS 2717	Pain	41.72	High
IAPS 9582	Pain	42.5	High
PICS M9P10	Pain	43.75	High
IAPS 3211	Pain	47.97	High
IAPS 9590	Pain	49.06	High
IAPS 3180	Pain	53.44	High
IAPS 3215	Pain	58.28	High
IAPS 3160	Pain	58.44	High
IAPS 9599	Pain	59.53	High
IAPS 3185	Pain	61.41	High
GAPED H083	Pain	61.43	High
IAPS 3191	Pain	65.94	High
GAPED H064	Pain	67.5	High
IAPS 3195	Pain	69.53	High

IAPS 8230	Pain	71.25	High
GAPED HO38	Pain	72.34	High
IAPS 3181	Pain	72.66	High
IAPS 9042	Pain	73.59	High
IAPS 3103	Pain	76.25	High
IAPS 3030	Pain	82.81	High
IAPS 3213	Pain	86.09	High
IAPS 9405	Pain	90	High
IAPS 3150	Pain	91.25	High

3.4.4.3 Threat Value

The full stimulus set comprising images split into 'Low Threat', 'Medium Threat and 'High Threat' categories are displayed in **Table 3.13** below. Of the 102 images, 24 fell into the Low Threat Category, 54 fell into the Medium Threat Category and 24 fell into the High Threat Category.

Table 3.13: Images by Threat Value Category with Means.

IMAGE NAME	*Stimulus Category*	*Mean Threat Value Rating*	*Threat Value Category*
IAPS 7950	Neutral	0	Low
IAPS 7004	Neutral	1.26	Low
IAPS 7035	Neutral	2.13	Low
IAPS 7003	Neutral	2.15	Low
GAPED N017	Neutral	2.96	Low
IAPS 7175	Neutral	3.02	Low
IAPS 7001	Neutral	3.04	Low
IAPS 7081	Neutral	3.26	Low
GAPED N106	Neutral	3.64	Low
IAPS 7057	Neutral	4.1	Low
IAPS 7002	Neutral	4.18	Low
IAPS 7052	Neutral	4.18	Low
IAPS 7009	Neutral	4.92	Low
IAPS 7211	Neutral	4.93	Low
PICS F2N1	Neutral	5.1	Low
GAPED N035	Neutral	5.11	Low
IAPS 7041	Neutral	5.26	Low
GAPED N107	Neutral	5.35	Low
IAPS 7032	Neutral	5.39	Low
IAPS 7006	Neutral	5.58	Low
GAPED N041	Neutral	5.84	Low
PICS F1N1	Neutral	6.01	Low
GAPED N061	Neutral	6.14	Low
PICS F10N1	Neutral	6.36	Low
GAPED N019	Neutral	6.61	Medium
PICS M8N2	Neutral	6.65	Medium

GAPED N097	Neutral	6.78	Medium
GAPED N009	Neutral	7	Medium
GAPED N020	Neutral	7.1	Medium
GAPED N027	Neutral	7.28	Medium
GAPED N092	Neutral	7.34	Medium
PICS F7N1	Neutral	7.36	Medium
GAPED N079	Neutral	7.4	Medium
PICS F4N1	Neutral	7.5	Medium
IAPS 7021	Neutral	8.16	Medium
GAPED N098	Neutral	8.17	Medium
PICS F11N2	Neutral	8.21	Medium
PICS F13P6	Pain	8.3	Medium
PICS F13N1	Neutral	8.73	Medium
PICS F9N1	Neutral	8.91	Medium
GAPED N089	Neutral	9.25	Medium
GAPED N014	Neutral	9.4	Medium
IAPS 7150	Neutral	9.51	Medium
PICS F4P1	Pain	9.66	Medium
PICS M7N1	Pain	9.76	Medium
IAPS 7080	Neutral	10.03	Medium
PICS F1P6	Pain	10.19	Medium
PICS M10N1	Neutral	10.19	Medium
PICS M6N1	Neutral	10.22	Medium
PICS M5N1	Neutral	10.31	Medium
PICS F11P2	Pain	10.39	Medium
GAPED N046	Neutral	10.97	Medium
PICS M2N1	Neutral	11.28	Medium
GAPED N085	Neutral	11.91	Medium
PICS F7P8	Pain	11.92	Medium
PICS M4P8	Pain	12.67	Medium
IAPS 7050	Neutral	13.04	Medium

PICS F9P7	Pain	13.15	Medium
PICS F2P4	Pain	13.42	Medium
PICS M2P9	Pain	13.71	Medium
PICS F6N1	Neutral	13.89	Medium
PICS M7N1	Neutral	14.31	Medium
PICS F6P7	Pain	14.35	Medium
PICS M10P1	Pain	14.35	Medium
PICS M5P1	Pain	14.98	Medium
PICS M4N1	Neutral	15.14	Medium
IAPS 7012	Neutral	15.15	Medium
PICS M9P10	Pain	15.33	Medium
IAPS 7016	Neutral	15.43	Medium
PICS F5N1	Neutral	16.12	Medium
PICS F10P2	Pain	16.48	Medium
PICS M8P8	Pain	16.59	Medium
PICS M3P9	Pain	16.8	Medium
PICS M6P2	Pain	17.25	Medium
PICS F5P4	Pain	17.3	Medium
PICS M1P1	Pain	17.46	Medium
IAPS 7030	Neutral	18.34	Medium
GAPED H095	Pain	19.02	Medium
IAPS 3280	Pain	22.61	High
IAPS 9582	Pain	23.8	High
IAPS 3215	Pain	24.68	High
IAPS 3185	Pain	27.01	High
IAPS 3180	Pain	27.08	High
IAPS 9599	Pain	27.13	High
IAPS 3160	Pain	27.67	High
GAPED H083	Pain	28.27	High
IAPS 3181	Pain	28.7	High
IAPS 3103	Pain	29.45	High

IAPS 9590	Pain	29.65	High
IAPS 3211	Pain	29.72	High
IAPS 3150	Pain	29.85	High
IAPS 8230	Pain	29.89	High
IAPS 9402	Pain	30.28	High
IAPS 2717	Pain	30.36	High
IAPS 3195	Pain	31.18	High
GAPED HO38	Pain	32.11	High
IAPS 3030	Pain	32.27	High
GAPED H064	Pain	32.51	High
IAPS 3213	Pain	32.56	High
IAPS 9592	Pain	32.8	High
IAPS 9042	Pain	33.14	High
IAPS 3191	Pain	33.71	High

3.4.5 Supplementary Analyses

3.4.5.1 Normative Ratings, DASS-21 and RPEQ (Composite) Scores

To examine whether the DASS-21 and/or RPEQ scores were related to the normative ratings for each image, a series of Pearson's R correlations were conducted. For the purposes of this analysis, the average Pain Intensity, Threat Value, Positive Valence, Negative Valence and Arousal were calculated for each individual participant across all 105 images. No significant correlations were observed between Depression, Anxiety and Stress and any of the normative ratings (p >.05). Similarly, no significant correlations were observed between composite RPEQ scores and any of the normative ratings (p >.05).

3.5 Discussion

The aim of this study was to validate pain/injury-related and neutral images from three already existing broad-topic databases (IAPS, GAPED, PICS), and generate measurements of their emotional properties (valence, arousal, threat value and pain intensity), to increase ecological validity of potential pain stimuli and enable better investigation of attentional biases (AB). These analyses revealed that, generally, pain/injury images possessed significantly higher ratings of pain intensity, threat value, arousal and negative valence compared to the neutral images. Analyses further enabled stimuli to be split by pain intensity (neutral = 47, low = 22, high = 23) and threat value (low = 24, medium = 54, high = 24). Albeit neutral stimuli were removed from each stimulus set for either possessing a low pain intensity (n = 13) or a high threat value (n = 3). Thus, a pain intensity stimulus set of 92 images and a threat value stimulus set of 102 images have been developed from merging existing databases that can now be used to test key claims of pain theories (e.g., Threat Interpretation Model, Todd et al., 2015). No relationship was found between self-reported Depression, Anxiety, Stress and Recent Pain Experiences and the normative ratings of the images. Results will now be discussed.

Many researchers exploring AB within the field of pain have relied upon the use of sensory and affective pain words (e.g., Deghani et al., 2003; Sharpe, et al., 2009; Liossi et al., 2009; Haggman et al., 2010; Schoth et al., 2018, 2019), with research generally finding significant ABs for sensory-pain words as opposed to affective-pain words (e.g., Haggman et al., 2010; Deghani et al., 2003). Considering the findings of Dear et al. (2011), the present study provides a fruitful avenue for future research to use pain-related pictorial stimuli to measure AB in pain. To recap, Dear et al., (2011) found that stimulus-related factors, including personal relevance and ecological validity, impact the ability to detect AB. Given the stimuli in the present study are idiosyncratically selected to measure ABs in individuals with pain, they can be argued to contain a higher personal relevance to these individuals. Consequently, these stimuli possess greater utility than word stimuli for measuring pain-related attentional biases in acute and/or chronic pain populations (see here also Maratos & Pessoa, 2019). That said, other stimulus related factors are also important. For example, the extent to which pain aspects of these stimuli or, alternatively their threat value influence ABs remains unknown. Hence, to increase personal relevance, ecological validity, and more rigorously measure pain-related ABs, the extent to which pain intensity and threat value exert their influence over pain-related ABs requires further examination. This can now be achieved given the stimuli produced in this research have both threat and pain intensity ratings.

Broad-topic databases can be criticised for not containing sufficient pain stimuli, which limits the extent to which pain biases and the key claims of pain theories can be examined. This was made evident by the fact that 16 stimuli previously rated as neutral, were rated as of low pain intensity or of a high threat value by participants in this study and thus were removed given their ambiguity of what they represent. Furthermore, of the studies that do use pain stimuli images, emotional properties including pain intensity, threat value, valence and arousal are not assessed. That research has found emotional properties including valence and arousal contribute to negative emotions, which subsequently influence pain perception (Godinho et al., 2008; Rhudy et al., 2007), emphasises the importance of normative ratings for stimuli used in pain studies - so that the effects of these aspects of stimuli properties (as opposed to their pain intensity) can be assessed.

Indeed, to better understand and disentangle pain effects from unpleasant affective states associated with pain images, pain intensity and threat value are of equal importance. Before the present study, a database containing a set of pain/injury and neutral images with measures of their emotional properties (pain intensity, threat value, valence, and arousal) was lacking. However, combining the images from three broad-topic databases has enabled the development of two new stimulus sets (pain intensity, threat value), to investigate and measure attentional processing in individuals with acute/chronic pain, and gain a more detailed insight as to the extent to which the pain aspects of these stimuli, or their threat value, influence ABs more rigorously.

For example, the TIM (Todd et al., 2015) proposes that once an individual interprets a stimulus as pain-related, attentional biases depend on the perceived threat value. Low threat leads to easy disengagement, moderate threat leads to difficulties with disengagement and high threat leads to avoidance. Hence, interpreting a stimulus as pain-related and subsequently threatening is proposed to influence the type of AB displayed (e.g., vigilance AB - medium, avoidance AB - high). Yet, the level of threat associated with pain-related stimuli (whether that be words or images) and their perceived pain intensity has not previously been investigated, as currently available stimulus sets do not contain ratings of pain-intensity. Given that the present study has developed categories pertaining to both pain intensity and threat value, theoretical predictions of such models can now be examined. For example, a high threat value, high pain intensity image should capture attention to a greater extent than a high pain intensity, but lower threat value image. The new stimulus sets developed as part of the present study enable such theoretical claims to be rigorously investigated, with low, medium, and high threat, and neutral, low and high pain intensity categories of stimuli, developed.

Finally, self-report measures including the DASS-21 and RPEQ were obtained in the present study and did not share a relationship with any of the normative ratings for the 105 images. This is somewhat consistent with Godinho et al. (2008) who observed no change in participants' rating of unpleasant pictures following their subjection to acute experimental pain. Hence, the normative ratings provided for the stimulus sets are not confounded by participants mood state (i.e., depression, anxiety, stress symptomology) or recent pain experiences. That said, a simple

explanation for these findings is that the sample in the present study possessed relatively low levels of Depression, Anxiety, Stress (DASS-21) and Pain (RPEQ).

3.5.1 Limitations

A limitation of the present study is that measures of test re-test reliability were not included. This would have been useful to see if normative ratings were consistent over time, particularly as research suggests that repeated exposure of images can increase one's sensitivity to those images, typically exhibited via exaggerated emotional responses when negative stimuli are displayed of a higher frequency/duration (Bradley et al., 1996; Smith et al., 2005; Dan-Glauser et al., 2011).

Additionally, a second limitation concerns the measure of arousal. In the present study, arousal was measured via a simple self-report statement – "How strongly does this image make you feel?" (0 – not at all, 50 – somewhat, 100 – very). It can be argued that measuring arousal in this manner is not optimal. Objective methods that measure physiological arousal, that is, the nervous systems response to real or perceived threat, may be preferred (Baird et al., 2021). To expand, research within the field of pain has demonstrated that the experience of pain can influence the sympathetic and parasympathetic branches of the autonomic nervous system (Kyle and McNeil, 2014). When an individual is aroused via a pain-related stimulus, research has demonstrated activity in the sympathetic nervous system resulting in increases in sweating, respiration, heart rate, blood pressure, muscle tension and pupil dilation (Norton & Asmundson, 2003). There are various ways to measure autonomic arousal, for example, via measurement of skin conductance, heart rate variability and/or pupil dilation, each of which may provide robust and objective (compared with subjective) capture of arousal. Indeed, considering that emotion has been divided into three components, known as the 'emotional response triad' (Scherer, 2001) comprising physiological arousal, motor expression, and subjective feeling, it is plausible to suggest that a combination of objective and subjective measures of arousal would have been optimal in the present study (i.e., self-report and physiological measures).

3.5.2 Conclusion

In summary, the present study provides normative ratings of pain intensity, threat value, valence (positive, negative) and arousal for 105 images (45 pain/injury images and 60 neutral images) obtained from three broad-topic databases, IAPS, GAPED and PICS. This has enabled two stimulus sets to be developed from the merging of these prior existing image stimulus sets, these are a stimulus set based upon pain intensity (n = 92) consisting of neutral, low pain intensity or high pain intensity and a stimulus set based upon threat value (n = 102) consisting of low threat, medium threat, or high threat ratings, respectively. The present study therefore addresses previous issues associated with ecological validity, lack of sufficient stimuli and a lack of consideration of emotional properties in the study of (chronic) pain. To sum, these 'new' stimulus sets offer increased flexibility to researchers, enabling them to select images based on their own design needs and research questions. Hence, these images can now be reliably used in pain research to investigate AB and test the key claims of pain theories (e.g., TIM, Todd et al., 2015) more rigorously.

Chapter 4 **Measuring Interpretation Bias using Ambiguous Scenarios in Adults: A stimulus-validation study.**

4.1 Introduction

Theoretical models of pain suggest that cognitive processes are implicated in the aetiology and maintenance of chronic pain (Vlaeyen & Linton, 2000; Eccleston & Crombez, 1999, 2007; Pincus & Morley, 2001; Van Damme et al., 2011; Todd et al., 2015; Van Ryckeghem et al., 2019). This includes the tendency to interpret ambiguous information in a pain and/or illness-related fashion (***this is Interpretation Bias, IB***). Interpreting ambiguous information in a pain-related manner is thought to contribute to the development and maintenance of chronic pain via increased pain catastrophising and fear of pain (Khatibi et al., 2014, 2015), both of which promote fear-avoidance behaviours (Buer & Linton, 2002; Andersen et al., 2016) that actively discourage individuals from undertaking everyday activities that promote recovery (e.g., exercise), contributing to increased disability (Elfving et al., 2007; Gheldof et al., 2010). In their review, Schoth and Liossi (2016) synthesised the results of seven studies investigating IB for ambiguous information in chronic pain patients and healthy controls. In all studies, chronic pain patients, relative to healthy controls, were found to be significantly more likely to interpret ambiguous words and facial expressions in a pain/illness-related fashion, with data for four out of the seven studies possessing a medium effect size.

Nevertheless, numerous methodological limitations of the paradigms used to measure IB have been highlighted. To expand, indirect measures of IB (e.g., Incidental Learning Task, Khatibi et al., 2014; 2015) have been criticised for lacking ecological validity due to the use of morphed facial expressions that do not reflect facial expressions in real life (Schoth and Liossi, 2016). Moreover, direct measures of IB, including the homographic response task (McKellar et al., 2003), homophonic response task (Pincus et al., 1996), and word-stem completion task (Edwards & Pearce, 1994; Griffith et al., 1996) suffer from a small number of appropriate stimuli. Additionally,

homophones have been argued to have differences in frequency of use (e.g., 'pain' has a higher written frequency than 'pane'), which reduce the likelihood of observing between-group differences (Francis & Kucera, 1967). Word stimuli further lack contextual information which, subsequently, raises concern over their personal relevance and ecological validity.

To develop a more rigorous, and direct measure of IB, Heathcote et al., (2016, 2017) designed the Adolescent Interpretation of Bodily Threat task (AIBT) using ambiguous scenarios as stimuli describing real-world contextual situations where it is unclear what is happening. To expand, the AIBT involves participants being presented with eight scenarios describing ambiguous situations that can be interpreted as relating to bodily-threat or pain (e.g., ***"Your dad jumps out of his chair and puts his hands to his face, making a loud noise. He is..."),*** and eight scenarios describing ambiguous social situations (e.g., ***"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..."***). Upon scenario presentation, participants are instructed to imagine themselves in the scenario, prior to being offered two solutions that resolve the scenario in a negative (e.g., "***Hurt"/ "Ridiculous"***) or benign (e.g., ***"Surprised" / "Important"***) manner. Next, participants are required to rate the following: i) how likely each interpretation was 'likely to enter their mind'; ii) which solution most likely 'popped into their mind'; and iii) their belief that each interpretation was a 'true reflection of reality'.

Two studies by Heathcote et al., (2016, 2017) found evidence of a significant negative IB. In study one, adolescents who reported higher levels of pain catastrophising endorsed negative interpretations across scenarios describing pain/bodily-threat and social situations. In study two, adolescents with chronic pain were found to be significantly less likely to endorse benign interpretations of pain and bodily-threat scenarios compared to their non-pain counterparts. Taken together, both studies provide evidence to suggest that the AIBT is an effective measure of IB in youth.

Relatedly, Lau et al. (2019) used an adapted version of the AIBT task in adolescents with persistent/interfering pain. This involved doubling the initial AIBT stimulus set to 16 items describing ambiguous situations around bodily harm - of which eight described immediate bodily

harm (i.e., potential injury) and eight described longer-term bodily harm (i.e., potential illness). An example of a longer-term bodily harm scenario is, "*When you wake up you notice that your eyes are swollen, and it is difficult to open them. You must be… **allergic***". Additionally, 16 items describing social situations were also included, eight of which described social evaluation and eight which described performance failure. An example of a performance failure scenario is, *"Your Maths teacher has decided to give a surprise test. You are sure that you will do… **badly**"*. In addition to the increased scenario set, Lau et al., also simplified the response format so that participants simply reported the degree to which each negative/benign solution was likely to explain the scenario presented using a 5-point Likert-type scale. Findings revealed that adolescents with low and moderate-to-high pain interference endorsed more negative interpretations across all situations (i.e., bodily harm and social threat) and were less likely to display a benign interpretation style compared with their non-pain interfering counterparts. Lau et al. concluded that adolescents with persistent pain display a negative IB for ambiguous bodily-harm and social evaluation situations, supporting the previous work of Heathcote et al. (2016, 2017).

Considering the above, a clear advantage of the AIBT is that it enables researchers to examine the context-specificity of biases. For example, do patients with chronic pain display biased interpretations of information related to bodily threat, pain or illness? Chan et al. (2020) demonstrated exactly this using the AIBT. That is, adults with chronic pain, as compared to their healthy counterparts, displayed a negative endorsement bias for ambiguous scenarios relating to immediate bodily injury and long-term illness. However, the AIBT is not without criticism. Firstly, the use of a forced-choice response format is questionable, given that it may not reflect the participants' own interpretation of the scenario. Thus, it is not yet known whether a forced-choice response format is optimal for measuring IB. Secondly, the lack of inclusion of 'filler' (i.e., neutral) scenarios increases the likelihood of demand characteristics and priming (e.g., towards pain interpretation). Thirdly, while ambiguous scenarios have demonstrated suitability in youth, it remains unknown whether these scenarios are appropriate for use in adult populations.

Hence, the purpose of the present study was threefold; i) to develop an AIBT task using free and forced-choice response formats, ii) to develop a set of ambiguous and "filler" (i.e., neutral)

scenarios and iii) to validate these for use with adult populations in pain research/treatment interventions. To achieve this, participants were first presented with a Word Generation Task (also known as a free response task). This required them to complete a set of ambiguous/filler scenarios by typing the initial word (or words) that came to mind. Second, participants completed a Likelihood Ratings Task (also known as a forced-choice task). This involved the presentation of two different solutions (one pain/pain-illness related, one non-pain/non-pain illness related) for each ambiguous/filler scenario, and participants to rate how likely they would be to use each solution to complete the scenario. Lastly, participants' pain experiences in the preceding 3 months were also measured, and the DASS-21 completed. This was to assess whether those that reported more recent pain experiences displayed differential task responding (and would support validity of the newly developed stimulus sets).

4.2 Materials and Methods

4.2.1 Participants

Participants were recruited via distribution of a study advertisement both physically (circulated on-campus) and electronically. This advert stated inclusion criteria of fluency in English, normal or corrected-to-normal vision and age of 18 or over; and resulted in recruitment of an opportunity sample of 521 participants from the University of Derby and wider UK general population. However, 278 participants (53.36%) were excluded from the analysis due to providing incomplete responses. A further two participants were excluded for violating the age-related exclusion criteria. Thus, the final sample comprised 241 participants, including 55 males (23.23%), 181 females (74.68%) and 5 who preferred not to declare their gender (2.07%). The age of participants ranged from 18 to 79 years ($M = 28.88$, $SD = 10.83$). The top four participant nationalities included British (32.37%), American (22.40%), Australian (6.64%) and Canadian (5.81%). English was the first language of most of the sample (78.4%). 52.7% of the total sample indicated that they had not been previously diagnosed with anxiety and/or depression.

Prospective power analysis using G*Power indicated that to achieve a medium effect size (.50) and acceptable power (i.e., 0.8; with alpha set at 0.05, one-tailed) for a repeated measures design, the calculated sample size required was 27. This power analysis was conducted based on one repeated-measures factors (scenario type, with two levels; ambiguous, filler). For compensation of their time and commitment to the study, students (24.06%) received course credit. Participants from the wider UK population were entered into a prize draw to win a £20 Amazon Voucher. The study was approved by the local Human Sciences Research Ethics Committee (HSREC) and informed consent gained from each participant prior to participation.

4.2.2 Design

The study conducted online to encourage a wide variety of demographics, employed a within-subjects design. The independent variable (scenario type) had two levels: ambiguous and filler (control). Participants completed two tasks: a Word Generation Task and a Likelihood Ratings Task for both ambiguous and filler scenarios. These tasks were not counterbalanced to avoid priming participants. To expand, solutions provided in the Likelihood Ratings Task (Pain/Pain-illness and/or Non-Pain/Non-Pain illness) could have inadvertently influenced responding to the Word Generation Task. Hence, the Word Generation Task was completed first by all participants.

4.2.2.1 Word Generation Task

In the word generation task, participants were presented with one of the ambiguous or filler scenarios in the centre of the screen in a randomised order. For example;

‘A bee lands on you and … your hand’

Participants were instructed to type a response in a box using the first word (or words) that came into their mind (e.g., ‘stings’, ‘tickles’). Each scenario was presented in 11.5 sized Helvetica font. Once participants had provided responses to all 62 scenarios the task was complete.

4.2.2.2 Likelihood Rating Task

In the likelihood rating task, participants were presented with one of the ambiguous or filler scenarios in the centre of the screen in a randomised order. This time, however, two-word solutions appeared simultaneously. For pain/pain-illness scenarios, one pain or illness solution and one non-pain/non-pain illness related solution appeared with the ambiguous scenario. For example:

‘Your drop a kitchen knife on the floor. It … your foot’

Cuts

Misses

For filler scenarios two neutral solutions were offered instead. For example;

‘You arrive at the office to start the working day. You turn on the …’

Computer

Lights

Next, like the methodology of Heathcote et al. (2016, 2017) participants were required to indicate how likely they would be to use each solution to complete the scenario by assigning a likelihood percentage using a sliding scale ranging from 0% to 100%. As participants were asked to rate likeliness for each solution on a 0 – 100% scale, ratings were not mutually exclusive (i.e., if participants rated their likelihood of using the first solution to complete the scenario as 70%, they were not restricted to rating the second solution as 30% likely to complete the scenario). Each scenario was presented in the centre of a new screen in 11.5 sized Helvetica font. Once likelihood

ratings had been provided for the two new solutions for each of the 62 scenarios, the task was complete.

4.2.3 Materials

4.2.3.1 Stimulus Set Creation

To create stimuli for the above two tasks, a stimulus set comprising 62 ambiguous scenarios was collated. Of these, 42 were stimuli that would elicit variability among participants in terms of pain/pain-illness vs non-pain/non-pain illness interpretations (i.e., ambiguous) and 20 were designed to elicit variability in terms of only non-pain/non-pain illness interpretations (i.e., filler).

4.2.3.1.1 *Pain/Pain-illness vs Non-pain/Non-pain illness Scenarios*

Of the **42** scenarios produced, **12** (ambiguous scenarios) were sourced from previous research by Heathcote et al. (2016) and Lau et al. (2020). The remaining **30** (ambiguous) scenarios were generated by DG, FM and PS. This involved an iterative process of each author generating scenarios and those judged by all three authors as ambiguous (in that they could be interpreted in a pain/pain-illness or non-pain/non-pain illness manner), were added to the scenarios sourced from previous research (**12**) and included in the final ambiguous stimulus set (**42**). In example:

'You drop the kitchen knife onto the floor, it … your foot'

This scenario is ambiguous because there are at least two potential responses that reflect different interpretations. For instance, the word '**hits**' would reflect a pain-related interpretation and '**misses**' would indicate a non-pain related interpretation.

4.2.3.1.2 *Filler (Control) Scenarios*

The above process was repeated to further generate a set of entirely novel filler scenarios to act as 'control' stimuli to avoid demand characteristics or priming participants with the ambiguous scenarios. As for the ambiguous scenarios, the same three authors (DG, FM, PS) first generated

many filler scenarios and then selected scenarios on the basis that all agreed they appeared ambiguous but, importantly, non-pain/non-pain illness related. This resulted in 20 such scenarios. For example:

'Your partner was late to an important meeting. This is because they forgot their…'

This scenario is ambiguous as there are at least two potential responses, such as the words '**Phone**' and '**Keys**'. However, this scenario is also non-pain/non-pain illness related in that potential responses are very unlikely to reflect a pain/illness interpretation.

Therefore, in total, the study comprised of **62** scenarios. Of which, **42** were '**ambiguous**' but potentially pain/pain-illness related and **20** were '**filler**'; that is, not pain nor pain-illness related. In line with previous research (e.g., Pincus et al., 1996), the mean number of words of each scenario in the ambiguous (Md = 15, n = 42) and filler (Md = 14, n = 20) categories were matched/controlled for (p = .431).

4.2.3.2 Self-Report Measures

4.2.3.2.1 *Recent Pain Experiences Questionnaire (RPEQ)*

To assess participant's subjective experiences of pain in the last three months, four items derived from the Brief Pain Inventory Short-Form were used (adapted from Cleeland and Ryan, 1994). Consistent with Heathcote et al. (2016) and Said et al. (2019) participants were required to rate their: i) average pain intensity; ii) worst pain intensity in the past 3 months (0 = no pain, 10 = worst pain possible); iii) the amount that pain had interfered with daily activities over the past 3 months (0 = I don't miss out on any activities; 10 = I miss out on all activities) and iv); the frequency of their pain over the last 3 months (1 = on less than 1 day each month, 10 = every day). The Brief Pain Inventory has been shown to be both reliable and valid across many cultures and languages (Cleeland & Ryan, 1994), and in the measurement of pain in numerous conditions including chronic non-malignant pain (Tan et al., 2004), osteoarthritis (Kapstad et al., 2010) and cancer pain (Kumar, 2011). Importantly, similar composite scores have further been used in previous research

measuring pain experiences in adult cancer patients (Ameringer, 2010) and aged populations (Parmelee et al., 1991).

4.2.3.2.2 *Depression, Anxiety and Stress Scale (DASS-21)*

To ascertain the endorsement of solutions was linked to pain as opposed to generalised anxiety/depression symptomology the DASS-21 (Henry & Crawford, 2005) was used. The DASS-21 is a 21-item questionnaire, comprised of 3 sub-scales of 7 items each: depression, anxiety, and stress. Participants are required to rate each item on a 4-point Likert-type scale ranging from 0 (does not apply to me at all) to 3 (applied to me very much, or most of the time), giving maximum possible sub-scale scores of 21 and a maximum total score of 63. To compare with the original DASS-42 scale, scoring instructions state total sub-scale scores should be doubled, and thus can range from 0-42. Research has tested the psychometric properties of the DASS-21 and found each sub-scale possesses adequate internal consistency, concurrent validity, and very good Cronbach's alpha values of .84, .74 and .79 for depression, anxiety and stress respectively (Antony et al., 1998; Musa et al., 2007; Asghari, et al., 2008; Wood, et al., 2010).

4.2.4 Procedure

The study was designed and completed using Qualtrics (Provo, UT). Participants were instructed that to participate they would need to complete the study individually in a quiet location and were required to confirm such conditions before the program moved on to the first task. Once confirmed and informed consent gained, participants provided demographic information then completed the Word Generation Task followed by the Likelihood Ratings Task. Once participants had completed both scenario tasks, they completed the *RPEQ* and the *DASS-21* questionnaires prior to being presented with a debrief. This included signposting to relevant support organisations in case of concerns (i.e., counselling helplines, pain concern). On average, the online study took participants 45 minutes to complete.

4.3 Results

4.3.1 Participant Characteristics

Descriptive data for the DASS-42 and REPQ are presented in **Table 4.1** below. A Mann-Whitney U test revealed no significant sex differences in depression ($p = .08$), anxiety ($p = .10$), stress ($p = .93$) or pain frequency ($p = .77$). Significant sex differences were observed for ratings of average pain U,(^{N}Males = 55, ^{N}Females = 181) = 3671.5, $z = -2.99$, $p < .01$, with females reporting more average pain ($Md = 2$) than males ($Md = 1$), worst pain intensity U, (^{N}Males = 55, ^{N}Females = 180) = 3652.5, $z = -2.80$, $p < .01$ than males, a higher worst pain intensity ($Md = 5$) than males ($Md = 3$), and greater interference of pain than males U, (^{N}Males = 54, ^{N}Females = 180) = 3532.5, $z = -3.12$, $p < .01$.

Table 4.1: Key Demographic Details and Means (SD) for the DASS-42 and Recent Pain Experiences Questionnaire.

DEMOGRAPHIC INFORMATION	
Age	28.88 (10.83)
Gender	**Males** = 55 (23.23%), **Females** = 181 (74.85%), **Prefer Not to Say** = 5 (2.07%).
Nationality (Top 5)	**British** = 78 (32.37%), **American** = 54 (22.40%), **Australian** = 16 (6.64%), **Canadian** = 14 (5.81%), **Other** = 79 (32.78%).
History of Anxiety and/or Depression	**Yes** = 104 (43.2%), **No** = 127 (52.7%), **Prefer Not to Say** = 10 (4.1%).
First Language	**English** = 189 (78.4%), **Other** = 52 (21.6%).
QUESTIONNAIRE INDICES	**MEAN (SD)**
Depression (DASS-42)	15.8 (10.64)
Anxiety (DASS-42)	9.93 (9.0)

Stress (DASS-42)	14.23 (12.01)
Pain Frequency (last 3 months)	3.16 (2.92)
Pain Intensity (last 3 months)	2.53 (2.20)
Worst Pain Intensity (last 3 months)	4.58 (3.11)
Pain Interference (last 3 months)	2.48 (2.83)
Recent Pain Experiences (Composite)	12.68 (9.57)

4.3.2 Word Generation Task (Free Response)

To identify the most ambiguous scenarios, solutions provided by all participants were organised into three different categories; pain/pain-illness, non-pain/non-pain illness, and difficult to define (DiD) by DG. See **4.2** below for definitions of each category. The percentage of solutions that fell into each of the three categories was calculated. This provided insight as to those ambiguous scenarios that were open to multiple interpretations (i.e., pain/pain-illness related, and non-pain/non-pain illness related).

Scenarios whereby the proportion of solutions fell overwhelmingly (>75%) or underwhelmingly (<75%) into the pain/pain-illness related or non-pain/non-pain illness related categories (i.e., were not ambiguous as to being pain-related or otherwise) were removed. Previous research by Heathcote et al. (2016) used parameters of <30% and >70%, however this can be argued to reduce stimulus set sizes to an unnecessary extent. Our slightly more lenient criteria ensured that only the most ambiguous scenarios were selected and resulted in the removal of 22 scenarios (#1-10, 13, 16, 20, 22, 24, 30-33, 35, 37, 39-41). Once scenario (#41), "*Yesterday your*

bicycle was hit by a car. You will not be able to cycle for a while because the car broke your…" narrowly missed the criterion, with 23.24% of solutions falling into the pain category and 75.93% into the non-pain/non-pain illness category. However, as response's reliability indicated one solution for the pain/illness category (that is, the word 'Leg' accounted for most of the pain responses, i.e., 34/56 responses i.e., 61%), the decision was taken to include this scenario. This resulted in 20 scenarios being included in the final stimulus set for word generation task validation (5, 7, 11, 12, 14, 15, 17-19, 21, 23, 25-29, 34, 36, 38, 42).

Table 4.2: Definitions used to categorise participant responses to the Word Completion Task.

Pain/Illness Definition	Non-Pain/Illness Definition	Ambiguous Definition

This category includes any word(s) or phrases that are indicative of immediate bodily harm (i.e., injury) or longer-term bodily harm (i.e., potential illness) to oneself or others, in context of the ambiguous scenario. Illnesses of an emotional and/or psychological nature (e.g., anxiety, depression) are not included in this category. Moreover, all professions associated with illness, disease and pain are included in this category (e.g., Dentist, Doctor, Optometrist etc.). Example: "You drop the kitchen knife onto the floor, it stabs your foot"	This category includes any word(s) or phrases that have no connection with immediate bodily harm (i.e., injury) or longer-term bodily harm (i.e., potential illness) to oneself or others. This category includes emotion-related words with positive/negative valence (e.g., Happy, Angry) and/or social-threat words (e.g., Embarrassed) in context of the ambiguous scenarios. Illnesses of an emotional and/or psychological nature (e.g., Anxiety/Depression) are included in this category). Example: "A bee lands on you and touches your hand"	This category includes any word(s) or phrases where: The word usage is unclear such that the word or phrase could be interpreted as fitting into more than one category. The word(s)/phrases offered do not make sense in context of the ambiguous scenario. Example: "You begin to breathe heavily. Your chest is quickly going up and down. You are dead"

Word Generation Task: Inter-Rater Reliability

To ensure DG's categorisation of responses generated by the participants in the Word Generation Task was consistent with the definitions outlined in Table 16, two members of DG's supervisory team (FM/PS) categorised responses to a sub-set (20%) of the ambiguous scenarios. Initially, inter-rater agreement with DG ranged from 79.41% (FM) to 77.81% (PS). However, following meeting and refinement of the definitions (e.g., addition of professions test to the Pain/Pain-illness definition), 100% inter-rater agreement was observed across all three raters.

Word Generation Task: Final Stimulus Set

A list of stimuli comprising the final scenario set for the Word Generation Task is presented below (**Table 4.3**). Note also, that the most popular pain/pain-illness and non-pain/non-pain illness answers generated by participants have been included for each scenario as footnotes. Here, in cases whereby the original pain/pain-illness and non-pain/non-pain illness solutions did not match the most popular answers generated by our participants to these scenarios, the offered solutions for each scenario were changed to reflect this. Scenarios labelled 'OLD' reflect those taken from previous research without changed solutions (n = 5), 'OR' representing 'old revised' reflects scenarios taken from previous research with changed solutions (n = 1), 'N' representing 'new' reflects new scenarios (i.e., those generated for purposes of the present study) without changed solutions (n = 8), and 'NR' representing 'new revised' reflects new scenarios generated for the purpose of this study with changed solutions (n = 6).

Table 4.3: A list of the full stimulus set generated from the Word Completion Task.

Word Completion Task: Final Stimulus Set	Status	Most Popular Pain/Pain-	Most Popular Non-Pain/Non-pain illness solution

		illness solution	
A ball hits you in the face. You look in the mirror and see your face is covered in…	**OLD**	**(Blood)**	**(Mud)**
You teach your child how to cut mushrooms on a polystyrene plate. You become distracted and notice they have cut through their…	**OLD**	**(Finger)**	**(Plate)**
You use scissors to cut out a picture from a piece of paper. Suddenly, your hand slips and you cut into…	**NR**	**(Your finger)**	**(The picture)**
Your friend Jenny is brushing her hair; it is really messy. When it gets stuck in a tangle, she…	**N**	**(Winces)**	**(Swears)**
You sit down at a team meeting and accidentally trap your… under the chair.	**NR**	**(Foot)**	**(Bag)**
You are playing football and your friend tackles you. You feel…	**N**	**(Hurt)**	**(Angry)**
You notice a red stain on your shirt. You are worried the stain won't come out because it is…	**NR**	**(Blood)**	**(Wine)**
You open a cupboard and a tin of baked beans falls out and hits…	**NR**	**(Your foot)**	**(The floor)**
You are playing sports with your brother; he runs into the house crying because you kicked the ball into…	**NR**	**(His face)**	**(The neighbour's garden)**

You see your neighbor close her car door and grimace. This is because she shut her … in the door.	**N**	**(Fingers)**	**(Dress)**
Your mother receives the health-practitioner test results she has been waiting for. Your mother is crying because she has received…	**N**	**(Bad news)**	**(Good news)**
You drop the kitchen knife onto the floor, it… your foot.	**N**	**(Hits)**	**(Misses)**
The wind blows a tile from your roof. It hits your…	**NR**	**(Head)**	**(Car)**
A bee lands on you and… your hand	**N**	**(Stings)**	**(Tickles)**
You slip and fall on some ice when running to catch the bus, you feel…	**N**	**(Hurt)**	**(Embarrassed)**
You go indoors after sunbathing. Your skin feels…	**N**	**(Burned)**	**(Hot)**
Yesterday your bicycle was hit by a car. You will not be able to cycle for a while because the car broke your…	**OLD**	**(Leg)**	**(Bike)**
You make an appointment to see your doctor to discuss your test results. You think the results will show you are...	**OLD**	**(Sick)**	**(Healthy)**
It is 10am on a Monday and you are still in bed. You are at home because you have a…	**OLD**	**(Cold)**	**(Day off)**
When you wake up your eyes are swollen and it's difficult to open them. This is due to...	**OR**	**(Allergies)**	**(Crying)**

4.3.3 Likelihood Ratings Task (Forced Response)

In recap, in this task the participants were required to rate the likelihood of a given solution occurring. Analysis here involved transforming data to calculate the total number of participants who rated the pain/illness solution (or the non-pain/non-pain illness solution) as the most likely to complete each scenario (e.g., 100% vs. 25%). A score of '1' was assigned to the participant solution rated as most likely to complete the scenario and a score of '0' was assigned to the participant solution that was least likely to complete the scenario; this enabled the identification of the stronger of the two endorsements. Below is an example of a participant's response to a scenario:

"*A ball hits you in the face. You look in the mirror and see your face is covered in…*"

Pain/pain-illness solution: **Blood**

Participant Likelihood Percentage: **100%**

Non-pain/Non-pain illness solution: **Mud**

Likelihood Percentage: **25%**

In this case, the pain/pain-illness solution (i.e., Blood) is assigned a score of '1' and the non-pain/non-pain illness solution (i.e., Mud) is assigned a score of '0' because the participant has rated the pain/pain-illness solution as most likely to complete the scenario. Scores were then summed across all participants for each solution and converted into a percentage. In cases where participants rated the pain/pain-illness related and non-pain/non-pain illness related solutions as equally likely to end the sentence for the scenario (i.e., 50% and 50% respectively), this data was removed and excluded from the final percentage calculation.

Scenarios were then selected based on two stages. First, scenarios whereby over 25% and under 75% of participants had chosen the non-pain/non-pain illness related solution to complete the scenario were selected for (as these represent ambiguity). This removed 14 scenarios (#1-3, 9, 10, 12, 20, 22, 29-33, 39) for which participants were either very likely to choose the pain/pain-

illness related solution (i.e., <25% non-pain/non-pain illness choice) or very likely to choose the non-pain/non-pain illness solution (>75% non-pain/non-pain illness choice); and so not ambiguous as to pain-related or otherwise. This left a sample of 28 scenarios for validation.

4.3.4 Reliability Analyses

A series of analyses were performed on the likelihood ratings data for the remaining 28 ambiguous scenarios. Each analysis was conducted with the full set of the 28 remaining scenarios, to produce an optimal number of robust scenarios.

4.3.4.1 Likelihood Ratings: Forced-Choice Data Analysis

In accordance with previous research (Heathcote et al., 2016), reliability analyses were carried out by using Cronbach's Alpha on the Likelihood Ratings Data for the pain/pain-illness solutions for the 28 scenarios. These revealed the scenarios to possess good internal consistency ($\alpha = .881$). However, several scenarios had item-total correlations below optimal ($r < .2$). Sequential removal of four scenarios (#8, 26, 20, 7) improved item-total correlations, with the remaining 24 scenarios correlating well with the total scale to an acceptable degree (lowest $r = .33$, $\alpha = .882$).

The non-pain/non-pain illness solutions also possessed good internal consistency ($\alpha = .854$). However, several scenarios had inter-item correlations below optimal ($r < .2$) suggesting they should be removed. Removal of one scenario (#26) improved the overall internal consistency ($\alpha = .856$) of the scenarios. The removal of 3 further scenarios (#9, 24, 28) that had item-total correlations below $r < .2$ did not improve the item-total correlations or the alpha value returned. Consequently, these items were not removed.

Thus, the Likelihood Ratings reliability analyses indicated 23 ambiguous scenarios were fit for purpose.

4.3.4.2 Likelihood Ratings: Internal Consistency (Forced-Choice Data)

To obtain a measure of internal consistency for the pain/pain-illness solution data for the 28 scenarios, the Kuder-Richardson Formula 20 (KRF-20) was used, as data was dichotomous. Overall, the 28 scenarios had acceptable internal consistency (α = .65). However, multiple scenarios had item-total correlations below optimal (r < .2). Sequential removal of 9 scenarios (**7, 10, 26, 20, 8, 24, 16, 9, 28**) improved overall internal consistency (α = .74). Deletion of further scenarios with correlations of r < .3 did not affect the alpha level returned, consequently these scenarios were not removed (see **Appendix 21**).

The KRF-20 was also used to analyse the non-pain/non-pain illness solution data for the remaining 28 scenarios. Overall, the scenarios had acceptable internal consistency (α = .64). However, multiple scenarios had item-total correlations below optimal (r < .2). Sequential removal of 9 scenarios (**7, 10, 26, 20, 8, 24, 28, 9, 16**) improved overall internal consistency (α = .72). Deletion of further scenarios with correlations of r < .3 did not affect the alpha level returned, consequently these scenarios were not removed.

Taken together, the reliability and KRF-20 analyses highlighted 9 scenarios as problematic (#**7-10, 16, 20, 24, 26, 28**). These included the 4 identified in the Cronbach's Alpha analyses as problematic **(#8, 26, 20, 7).** Thus leaving 19 ambiguous scenarios. However, one further scenario (**#5**) was also removed due to the pain/pain-illness solution of 'fearful' being difficult to categorically define as pain-related (vs. anxiety related) according to our definitions. Therefore, this scenario was also removed resulting in the second stimulus set comprising 18 scenarios. These are presented in **Table 4.4**, where 'Old' represents scenarios taken from previous research (Heathcote et al., 2015, 2016; Lau et al., 2019, N = 8) and 'New' represents scenarios developed for purposes of the present study (N = 10).

Table 4.4: A list of the full stimulus set generated from the Likelihood Ratings Task.

Likelihood Ratings Task: Final Stimulus Set	Pain/Illness Solution	Non-Pain / Illness Solution	Status
You wake up and notice how you feel today. You feel…	Sore	Refreshed	**N**
A ball hits you in the face. You look in the mirror and see your face is covered in…	Blood	Mud	**OLD**
Your cousin visits the doctor to get his test results back. His growth is…	Cancerous	Benign	**OLD**
You teach your child how to cut mushrooms on a polystyrene plate. You become distracted and notice they have cut through their…	Hand	Plate	**OLD**
You use scissors to cut out a picture from a piece of paper. Suddenly, your hand slips and you cut into…	Your Finger	The picture	**N**
You notice a red stain on your shirt. You are worried the stain won't come out because it is…	Blood	Pen	**N**
You open a cupboard and a tin of baked beans falls out and hits…	Your head	The floor	**N**
You are playing sports with your brother; he runs into the house crying because you kicked the ball into …	His face	The neighbour's garden	**N**
You see your neighbour close her car door and grimace. This is because she shut her… in the door.	Fingers	Coat	**N**
Your mother receives the health-practitioner test results she has been waiting for. Your mother is crying because she has received…	Bad News	Good news	**N**
You drop the kitchen knife onto the floor, it … your foot.	Cuts	Misses	**N**
The wind blows a tile from your roof. It hits your…	Head	Car	**N**
A bee lands on you and … your hand.	Stings	Tickles	**N**
Yesterday your bicycle was hit by a car. You will not be able to cycle for a while because the car broke your…	Leg	Bike	**OLD**

Your Dad is driving you in the car. Suddenly your car hits the car in front of you. You are…	Hurt	Scared	**OLD**
You make an appointment to see your doctor to discuss your test results. You think the rest results will show you are …	Ill	Fine	**OLD**
It is 10am on a Monday and you are still in bed. You are at home because you have a …	Cold	Holiday	**OLD**
You begin to breathe heavily. Your chest is quickly going up and down. You are…	Asthmatic	Exercising	**OLD**

4.3.5 Filler (Control) Scenarios: Data Analysis

The filler stimulus set comprising 20 scenarios were tested for ambiguity. Given the nature of these scenarios, the criteria applied to the ambiguous scenarios set for the Word Generation and Likelihood Ratings Tasks were deemed unsuitable. Instead, scenarios were removed based upon several criteria. This included: i) if either of the two most popular solutions had positive or negative connotations; ii) the scenario was not ambiguous (i.e., the second most popular answer was disproportionately selected in that less than 10% of the sample generated this response); and iii) the two most popular answers for one scenario were identical to another scenario. After applying these criteria, 12 filler scenarios remained. Next, in cases where the two most popular solution(s) for the filler scenarios did not match the solutions initially generated by the researcher, the most popular solutions provided by participants were used as replacement. Of the 12 remaining scenarios, this led to 6 scenario solution changes (#3, 5, 6, 7, 10, 11).

4.3.5.1 Filler Scenarios: Final Stimulus Set

A list of the full filler scenarios is presented in **Table 4.5** below. To enable use in Likelihood Rating style tasks (as well as Word Generation tasks), the top two solutions for each scenario are provided. All 12 filler scenarios were generated for the purpose of the present study (i.e., none were obtained from previous research).

Table 4.5: A list of the full filler (control) scenarios set.

Filler Scenarios: Final Stimulus Set	Top Filler Solution 1	Top Filler Solution 2
You watch the weather forecast on the TV. Tomorrow it is forecast to be a … day.	**(Sunny)**	**(Rainy)**
You receive a letter from your child's head teacher. This was written using a …	**(Pen)**	**(Computer)**
You see some fish swimming in the water. They are swimming in a …	**(Pond)**	**(Circle)**
Your partner is late to an important meeting. This is because they forgot their …	**(Phone)**	**(Keys)**
You get home from work and realise you left the … on.	**(Light)**	**(Oven)**
After a long day, your grandmother likes to have a drink of …	**(Tea)**	**(Wine)**
You get distracted and when you return you realise you forgot to boil the…	**(Water)**	**(Kettle)**
During a chat, your younger sister tells you she wants to learn how to ride a …	**(Bike)**	**(Horse)**
You let your dog off the lead at the local park. Immediately your dog sprints to fetch a …	**(Stick)**	**(Ball)**
The postman brings you a delivery you had been expecting. You open the…	**(Package)**	**(Box)**
You look across the room and see your cat. He is sat on the…	**(Sofa)**	**(Mat)**
You arrive at the office to start the working day. You turn on the...	**(Computer)**	**(Light)**

4.3.6 Recent Pain Experiences and Likelihood Ratings Task.

Forty-three participants reported experiencing no pain in the preceding three months and therefore their scores on the RPEQ were transformed. That is, these participants were assigned the

following: a score of '0' for pain intensity; a score of '0' for interference; and a score of '1' for frequency, in accordance with Heathcote et al. (2016).

Next, the relationship between recent pain experiences and likelihood ratings for pain/pain-illness and non-pain/non-pain illness solutions for all scenarios on the Likelihood Ratings Task were assessed. There was a weak, significant, positive correlation between recent pain experiences and likelihood ratings for pain/pain-illness solutions $r = .164$, $n = 241$, $p = .005$, *one-tailed*. There was also a weak, negative, non-significant correlation between recent pain experiences and likelihood ratings for non-pain/non-pain illness related solutions $r = -.086$, $n = 241$, $p = .09$, *one-tailed*.

Simple linear regression with a composite recent pain experiences score as the predictor variable and likelihood ratings for the pain/pain-illness solutions as the outcome variable revealed that participant's recent pain experiences predicted likelihood ratings for the pain/illness related solutions $F(1, 240) = 6.61$, $p = .01$ with an R^2 of .027. So, recent pain experiences explained 27% of the variance in likelihood ratings for the pain/pain-illness solutions. That is, the more an individual had suffered with pain in the last three months the more likely they were to endorse pain/pain-illness solutions. However, when the likelihood ratings for the non-pain/non-pain illness solutions were included as the outcome variable, no significant regression equation was found $F(1, 240) = 1.78$, $p = .18$ with an R^2 of <.01. In other words, recent pain experiences did not explain any variance in the likelihood ratings assigned to the non-pain/non-pain-illness solutions.

4.4 Discussion

4.4.1 Overview

The aim of the present study was to develop an AIBT task using free and forced-choice response formats, with filler (i.e., "neutral") trials, suitable for use with adults to enable proper investigation of IB in pain research. This was achieved via the development of two ambiguous stimulus sets,

both possessing good internal consistency; a Word Completion (free-response) set, and a Likelihood Ratings (forced-choice) set. Further, 12 control scenarios were also validated to address limitations of previous research e.g., demand characteristics/priming. Thus, combining the scenarios for each response format and filler trials results in a stimulus set size of 32 (word completion stimulus set) and 30 (Likelihood rating stimulus set), respectively. Supplementary analyses revealed that adults who reported more recent pain experiences in the preceding 3 months further displayed an endorsement bias. To expand, adults with more recent pain experiences were significantly more likely to endorse using the pain/pain-illness solutions to complete the ambiguous scenarios presented in the Likelihood Ratings Task. Considering this, the utility of these ambiguous scenario sets for pain-related research as well as treatment programme efficacy evaluation will be discussed.

4.4.2 Implications

Previous direct measures of IB, including the Homographic/Homophonic response task (e.g., McKellar et al., 2003) have been criticised for a lack of appropriate stimuli and for failing to account for frequency of use (Schoth & Liossi, 2017). Paradigms such as the AIBT (Heathcote et al., 2016) address these limitations, but are not devoid of criticism given that participants are constrained by a forced-choice response format and lack of validation in adult samples. The use of forced-choice response formats is particularly problematic given that the solutions presented may not reflect the participants personal interpretation of the scenario. Consequently, it is unclear whether this format is a suitable and reliable measure of pain/pain-illness related IBs. Of novel value, the stimulus sets developed in this research support two response formats; forced-choice and free-response, and, additionally, are appropriate for adult populations. A further limitation of previous direct IB measures is that these measures run the risk of participants displaying response biases/demand characteristics (Schoth & Liossi, 2016). This is important as awareness of potentially threatening information can prime participant responding, including whether individuals attend to or avoid such information (Hedger et al., 2015; Lapate et al., 2014; Maratos & Pessoa, 2019). To expand, the sole presentation of ambiguous pain-illness/non-pain illness

scenarios may inadvertently influence participant responding (e.g., pain-related responding may prime further pain-related responding). Hence, the development of control scenarios in the present study and the ability to integrate these with the ambiguous pain-illness/non-pain illness scenario sets will help to circumvent this, as well as potential confounds of order effects and demand characteristics.

Thus, the present study has produced a 'forced-choice' or likelihood ambiguous scenario set comprising 30 scenarios (18 ambiguous; 12 control) that can be used in IB related research/treatment efficacy evaluation with adult populations. Moreover, a further 'word generation' or free-response scenario set has been developed containing 32 scenarios (20 ambiguous; 12 control). Given the limitations of previous forced-choice paradigms, these stimulus sets arguably possess greater utility in measuring pain-related IBs. Indeed, stimuli from both sets can be used as open-ended or free-response stimuli, avoiding limitations/constraints associated with forced-choice paradigms (Schoth & Liossi, 2017).

A further finding of the current study was that adults who self-reported more recent pain experiences were significantly more likely to assign a higher likelihood rating to pain/pain-illness related solutions (as opposed to non-pain/non-pain illness solutions). This is noteworthy given that it is in accord with previous IB research. To recap, Heathcote et al., (2016) found that adolescents who reported higher pain catastrophising and more recent pain experiences were more likely to endorse pain/illness-related interpretations (as opposed to benign interpretations) of ambiguous situations. A finding that was later replicated with adolescent chronic pain sufferers (Heathcote et al., 2017). Subsequent research by Lau et al., (2019) supports this notion, demonstrating that adolescents who reported moderate-to-high pain interference, compared to their non-interfering pain counterparts, displayed an endorsement bias for pain/illness interpretations. Further, Chan et al. (2020) recently found that adults with chronic pain displayed a negative endorsement bias for ambiguous scenarios. Our findings are thus consistent with such previous research, demonstrating that adults with acute and/or chronic pain favour pain/pain-illness related interpretations of ambiguous information. Taken together, these findings provide validation of the stimulus set

obtained from the Likelihood Ratings Data, and demonstrates they are fit for purpose to measure IB in Adults.

4.4.3 Methodological Considerations

A limitation of the present study was the inability to perform reliability investigations for the scenarios generated via the Word Generation Task, as participants were not constrained to a pre-determined list of interpretations. However, this is also a strength of the present study; that is, it enabled participants to generate novel solutions. Inter-rater reliability was not considered problematic as the agreement pertaining to the categorisation of participants responses was high, averaging 79.41% (FM) to 77.81% (PS) before discussion, and 100% after. This not only shows good validity of our categorisations; but also provides evidence of criterion validity for the Word Generation Task. A second limitation of the present study concerns the use of word stimuli. Word stimuli are argued to possess lower ecological validity than pictorial stimuli (e.g., pain-related facial expressions, Schoth & Liossi, 2017), given they require cognitive processing. That said, we argue this critique is of increased important when measuring ABs given that word stimuli may be limited in initial threat (or pain) value (Schimmack, 2005), which may influence the attentional processes displayed (Todd et al., 2015; Gaffiero et al., 2019). Moreover, the pictorial stimuli (i.e., morphed facial expressions) have been used in previous IB research (see Khatibi et al., 2014; 2015) they have been criticised for not being reflective of the facial expressions viewed in everyday life.

A third limitation concerns reporting bias. One valid criticism of all interpretation bias paradigms is that there are no objective means to ascertain whether a response provided by a participant is the response they had initially generated when confronted with ambiguity. Hence, participants may consciously (or unconsciously) modify their interpretation (e.g., due to demand characteristics). The present study actively attempted to reduce reporting bias via carefully worded task instructions, for example, instructing participants to type a response in a box using the "***first*** word (or words) that came into their mind". However, despite such task instructions, given that there are no objective means of ensuring participants provide the first solution generated, this remains a

limitation of the present study, but is also a critique of interpretation bias methodology more generally.

4.4.4 Future Research

The stimulus sets developed in the present study serve as important tools to measure IB in adults with pain. Additionally, they could also be incorporated with other paradigms to measure memory (recall and/or recognition) biases and the role recall/recognition biases play in acute/chronic pain. Here, for example, participants could be presented with both pain/pain-illness and non-pain/non-pain illness solutions for the Likelihood Ratings Task and investigation of which they recall at a later date probed. Recalling more solutions that reflect a pain/pain-illness interpretation, as opposed to a non-pain/non-pain illness interpretation, would provide evidence to suggest pain memory biases. Similarly, the Likelihood Ratings Task could also be used to investigate biases in recognition. Here, for example, participants could be presented with the Likelihood Ratings Task, and their solutions to each scenario presented back to them at a later date in the form of a Yes/No recognition paradigm. Using the Signal Detection Method, a measure of 'Hits', 'Misses', 'False Alarms' and 'Correct Rejections' could be obtained for the pain/pain-illness solutions and the non-pain/non-pain illness solutions. A significantly higher number of correct responses for pain/pain-illness solutions (i.e., 'Hits' and 'Correct Rejections') compared to incorrect responses (i.e., 'Misses' and 'False alarms') would provide evidence of biased recognition for pain/pain-illness related information. Until now, these experimental designs have not been possible due to the lack of validation of ambiguous scenarios in adult samples. Importantly, these brief future research examples highlight the adaptability and potential utility of the ambiguous scenarios and sets developed in the present study to advance knowledge regarding combined cognitive biases in pain.

Secondly, pain catastrophising appears to play a central role in the development and maintenance of chronic pain related disability (Vlaeyen & Linton, 2000; Eccleston & Crombez, 1999; Varallo et al., 2021; Giusti et al., 2020) and appears to be associated with IB in both clinical and control samples (Vancleef et al., 2009; Khatibi et al., 2014, 2015). Considering this, future

studies could test this association and evaluate whether interventions aimed at reducing pain catastrophising (e.g., Cognitive Behavioural Therapy) influence IBs.

4.4.5 Conclusion

The aim of the present study was to develop an AIBT task using free and forced-choice response formats with filler trials suitable for use with adults, to enable proper and rigorous investigation of IBs. Importantly, two separate stimulus sets that allow for two response formats, forced-choice (i.e., likelihood) and free response (i.e., word generation), were developed for use in pain/pain-illness IB research to address the limitations of previous research. Thus, the current study provides two new stimulus sets that can be utilised to measure pain/pain-illness related IBs in adults. For the forced-choice likelihood scenario task, supplementary analyses revealed that adults who reported more recent pain experiences over the past 3 months were more likely to assign a higher likelihood rating to the pain/pain-illness solutions, lending support to previous pain-related-bias research in this area (Heathcote et al., 2016, 2017; Lau et al., 2019; Chen et al., 2020). However, further research measuring multiple cognitive biases within the context of a single study is still needed; particularly to test key theoretical assumptions, including those of the Threat Interpretation Model (Todd et al., 2015) That said, the utility/flexibility of the Likelihood Ratings (free response) scenario set, including the ability to measure more than one bias (i.e., IB and MB) with these stimuli, will help to simplify the complex methodological processes often involved with measuring multiple cognitive biases.

Chapter 5 **Exploring the effects of Pain Manipulation on Attention, Interpretation and Memory Biases.**

5.1 Introduction

Cognitive biases have been implicated in psychological disorders, including anxiety and depression (Matthews, Mackintosh & Fulcher, 1998). Evidence for pain-related cognitive biases, namely attentional bias, interpretation bias, and memory bias can be described as mixed at best (see Chapter 1, section 1.4.4). Theoretical models of pain argue that cognitive biases operate in a cyclical fashion and interact with one another to impact pain chronicity (Van Ryckeghem et al., 2018; Todd et al., 2015). Yet, studies typically investigate pain-related cognitive biases in isolation (See Chapter 1, sections 1.4.1 to 1.4.3). Consequently, the interplay between these biases remains poorly understood. That said, one study has found preliminary evidence to support the notion that cognitive biases (specifically attentional biases) are implicated in the transition from acute to chronic pain (Lautenbacher et al., 2010). Here, a prospective longitudinal study was conducted to examine the predictive power of attentional and emotional variables (including attentional biases) for the development of chronic postoperative pain, following surgery to correct for chest malformation. Participants were assessed at three intervals: 1 day prior to surgery, 3 months post-surgery and 6 months post-surgery. Results showed that patients with high pain intensity at three and six-months post-surgery displayed an attentional bias for positive words in a dot-probe task completed 1 day prior to surgery. The authors postulated that such findings are indicative of individuals avoiding the necessary confrontation of pain, which increases the likelihood that these individuals will develop chronic post-operative pain.

However, as discussed in Chapter 1 (section 1.3), broader theoretical models diverge in their proposed sequential nature of these biases. To briefly recap, in the anxiety literature, the Combined Cognitive Bias Hypothesis (CCBH, Hirsch et al., 2006) argues that interpretation bias precedes attentional bias. Yet, the reverse is argued when considering depression (Everaert et al.,

2013). Considering pain, the Threat Interpretation Model (TIM, Todd et al., 2015) argues that once a stimulus is categorised as pain-relevant, the degree to which it influences attentional processes is dependent on whether the stimulus is interpreted as threatening. Low threat leads to easy disengagement, moderate threat to difficulty disengaging, and high threat to attentional avoidance. Similarly, Van Ryckeghem et al., (2019) recently developed the Integrated Functional Contextual Framework (IFCF) which proposes that early attention is captured by ambiguous bodily sensations, which are then interpreted as threatening or non-threatening. This impacts subsequent attentional processes and how situations are remembered, this then contributes to a memory bias. So, when similar bodily sensations are experienced in future, this pain memory becomes re-activated affecting attention and interpretation biases. That said, as research investigating combined cognitive biases is still in its infancy, these proposed relationships remain speculative.

To date, only a handful of researchers have explored pain-related attention (AB), interpretation (IB) and/or memory biases (MB) in chronic pain samples. Much like the wider cognitive bias literature, findings are mixed, with studies reporting no evidence for cognitive biases per se (e.g., Blaisdale-Jones et al., 2021), evidence for one cognitive bias such as interpretation (Chan et al., 2020; Chan et al., 2022), or evidence for multiple cognitive biases such as AB and IB (Hughes et al., 2017; Schoth et al., 2018), but not MB (Schoth et al., 2019). Fewer studies have investigated combined cognitive biases in acute pain samples, with Todd et al., (2015) the first to examine AB and IB, finding that experimentally manipulating threat in a laboratory environment does not influence these biases in healthy adults. Most recently, Chan et al., (2020) conducted a lab-based study examining the association between IB, AB and threat in healthy adults. Participants were given threatening or reassuring information about an upcoming cold-pressor task, IB was measured prior to this task, and AB was measured after using a free viewing paradigm. Findings showed that adults who exhibited a negative IB were more likely to assign a greater threat value to the cold-pressor task, additionally, those with higher levels of anticipated harm were more likely to explore scene images depicting injury. Indeed, further analyses demonstrated that anticipated harm mediated the relationship between IB and eye-movements. That said, no between-groups differences were observed in eye-movements with respect to the threatening

information received (threatening, reassuring). The authors concluded that IB may play a key role in attentional processing, highlighting the potential interplay between these biases.

A more recent systematic review of the eye-tracking literature with respect to attention and pain accord with the above experimental research of Chan et al., (2020), finding that biases for pain-related information are ubiquitous and not influenced by current pain status (Blaisdale-Jones et al., 2021). This supports the evolutionary account of attentional bias, with ABs for pain-related information serving an adaptive function by enabling an organism to rapidly detect potential situations that could result in bodily-harm; and thus enable the organism to adopt an appropriate protective response. These findings accord with models of pain. For example, the Cognitive Affective Model (Eccleston & Crombez, 1999) asserts that attention is a mechanism of selection for action where pain is selected for escape. Therefore, pain is ontogenetically and evolutionarily predisposed to interrupt attention to limit the impact of aversive events. Moreover, further theoretical models, including the previously mentioned IFCF (Van Ryckeghem et al., 2019), argue that context is a key determinant of the adaptive value of pain. This can be explored through the lenses of various model; for example, the Misdirected Problem-Solving Model (Eccleston & Crombez, 2007) asserts that if pain-removal becomes a focal goal, this can fuel AB and lead to a maladaptive cycle where attempts to remove pain fail and impede other life goals. In such cases, pain becomes attentionally prioritised per se, even when not relevant. Hence, the context within which pain exists is important.

With respect to memory bias, including recall and recognition, there has been evidence to suggest that individuals experiencing pain (acute or chronic) display enhanced recall and/or recognition of pain related stimuli (Pincus & Morley, 2001; Schwarze et al., 2012; Wimmer & Buchel, 2015). However, contradictory findings have emerged suggesting impaired recall and recognition of pain and/or neutral stimuli (Busch et al., 2006; Grisart et al., 2007; Forkmann et al., 2016). Albeit, considering the above it would be logical to posit that preferentially attending to one stimulus (e.g., pain) over another (e.g., neutral) would result in enhanced encoding, and potentially enhanced memory recall and recognition for that stimulus.

This said, it is important to acknowledge that to the author's awareness, no studies have measured cognitive biases both *prior to* and *after* experience of experimental pain (e.g., cold-pressor task, as outlined in Chapter 2, section 2.5) in the same study. This is important as it would allow one to disentangle whether a pain experience itself influences participants' cognitive processing. Indeed, investigating cognitive biases in this way would enable researchers to examine which biases (i.e., attention, interpretation and/or memory), if any, are influenced by an acute pain experience to further understand how pain influences cognitive biases. Additionally, investigating cognitive biases both ***prior to and*** after experience of pain enables testing of key predictions of the Threat Interpretation Model (TIM; Todd et al., 2015). Hence, further laboratory work in pain-free participants is needed to understand the basic mechanisms of how (or if) a painful experience influences cognitive biases.

Considering this, the present study investigated whether pain influences attention, interpretation and memory biases (recall and recognition) in a pain vs no-pain experimental situation. This allowed for the examination of whether pain influences biases selectively; e.g. attention to a greater extent than interpretation and/or memory. This is a potentially important starting point for understanding the relationship between pain and cognitive biases. Thus, in the present study, all participants were presented with a computerised Interpretation Bias Task (the Ambiguous Scenarios Stimulus set developed in Chapter 3) and then an Attentional Bias Task (comprising Free-viewing with the validated Pain Images developed in Chapter 4). Using random allocation, partcipants then took part in a cold-pressor task (the pain condition) ***or*** a warm water task (the no-pain condition). Following which they then completed modified 'second' versions of the Interpretation and Attentional Bias Tasks, a Recent Pain Experiences Questionnaire and a surprise free recall task. Finally, one-month post-experiment, participants completed an online recognition memory task (Yes-No paradigm) to measure the extent of memory biases over a longer retention period.

Based on literature introduced here and in Chapter 1, it was hypothesised that participants allocated to the pain condition would:

1) Interpret more ambiguous scenarios in a pain/pain-illness related manner in the second interpretation bias task after pain induction (cold-pressor), compared to their non-pain counterparts.
2) Display AB for pain-related information presented in the second freeviewing task after pain induction (cold-pressor), compared to their non-pain counterparts. More specifically, it was predicted that the type of AB displayed post pain induction would be influenced by the threat value of the pain stimuli:
    a. Participants in the pain condition would display a vigilance-avoidance pattern of processing for the High Pain (High Threat) images after pain induction, while those allocated to the No Pain condition would display normal attentional processing.
    b. Participants in the pain condition would display vigilance during early attention and difficulty disengaging in maintained attention for the Low Pain (Moderate Threat) images, while those allocated to the No Pain condition would display normal attentional processing.
3) Correctly recall a higher percentage of pain/pain-illness related solutions used in the second Interpretation Bias Task than their non-pain counterparts.
4) Correctly recognise more pain/pain-illness related solutions 1-month later compared to their non-pain counterparts. More specifically, participants in the pain condition would recognise more pain/pain-illness related solutions they generated in the second Interpretation Bias Task (post pain-induction) when asked to identify these one month later (using a yes/no paradigm).
5) Exhibit biases that influence and/or interact with one another. More generally, it was anticipated that relationships would emerge between Attention, Interpretation. Memory Biases and pain outcomes (Threshold, Tolerance, Average Pain) post the cold-pressor task.

5.2 Method

5.2.1 Participants

Participants were recruited via distribution of a study advertisement. This was achieved via the University of Derby's Psychology Research Participation System by email, and the use of printed advertisements placed in the University's on-campus coffee shop (Blends). This advert stated inclusion criteria of fluency in English, normal or corrected-to-normal vision, and of age 18 or over. This resulted in recruitment of an opportunity sample of 46 participants (students) from the University of Derby, exceeding the sample size obtained in previous combined cognitive bias research (e.g., Schoth et al., 2018: $n = 37$). Prospective power analysis using G*Power indicated that to achieve a medium effect size (.25) and acceptable power (i.e., 0.8; with alpha set at 0.05, one-tailed) for a repeated measures design, the calculated sample size required was 82. This power analysis was conducted based on one between-subjected variable (group, pain, no pain) and two within-subjects factors (manipulation; pre, post, stimulus type; ambiguous, filler). Participants were ineligible to participate if they were pregnant, reported the use of medication (except for hormonal contraception), or experienced any of the following: heart problems, peripheral neuropathy, circulatory disorders (i.e., Reynaud's disease) and/or unmedicated high or low blood pressure. Moreover, participants previously or currently diagnosed with a pain-related condition, for which they had received treatment to manage their pain, were also unable to take part.

In total all 46 participants undertook all phases of this study. The final sample compromised 14 males (30.44%) and 32 females (69.56%). The age of participants ranged from 18 to 56 years ($M = 22.46$, $SD = 7.6$). Most participants were British (71.74%), white (71.74%), listed English as their first language (73.91%) and did not have any history of anxiety and/or depression (70%). Participants were randomly assigned to the pain ($n = 22$) or no pain ($n = 24$) condition. For compensation of their time and commitment to the study, students (100%) received course credit. The study was approved by the Human Sciences Research Ethics Committee at the University of Derby and informed consent was gained from each participant. The study was conducted between

November and July 2021, when COVID-19 regulations had been relaxed in the UK to allow for face-to-face data collection.

5.2.2 Design

The study employed a mixed-measures design with six independent variables, including one between-subjects variable and five within-subjects variables. These were: (**1**) experimental condition (pain, no pain; between-subjects) and (**2**) pain manipulation (pre vs. post pain manipulation). Then, specific to the interpretation bias task, (**3**) scenario type (ambiguous, filler); specific to the attentional bias task (**4**) stimulus category (pain and injury related; comprising high pain, low pain, and neutral images); and specific to the memory bias tasks (**5**) word type (pain/pain-illness related, non-pain/non-pain illness related). The dependent variables included interpretation bias index scores (interpretation bias task), attentional bias index scores and eye-tracking indices (attentional bias task), the total number of words correctly recalled (memory bias - free recall task), and correct and incorrect recognition scores categorised via the signal detection method (memory bias – recognition task).

5.2.3 Materials

All participants completed each of the questionnaires detailed below.

5.2.3.1 Demographic Questionnaire

Participants reported on demographic details comprising age, gender, nationality, educational level, history of anxiety/depression (Yes/No response) and first language.

5.2.3.2 Depression, Anxiety and Stress Scale (DASS-21)

The DASS-21 scale was used (Henry & Crawford) as a control measure to investigate whether cognitive biases were reflective of pain as opposed to depressive and/or anxiety symptomology. The DASS-21 is a 21-item questionnaire, with 3 sub-scales comprised of 7 items to measure depression, anxiety, and stress. Item scores range from 0 (does not apply to me at all) to 3 (applied to me very much, or most of the time), giving a maximum possible sub-scale score of 21. Severity (i.e., normal, mild, moderate, severe, extremely severe) is interpreted via the scores for each sub-scale. Higher scores reflect greater severity. To enable comparison with the DASS-42, total scores for each subscale were doubled in accordance with the scoring instructions (Henry & Crawford, 2005). This scale has been found to possess favourable psychometric properties in clinical and non-clinical samples (Crawford & Henry, 2003).

5.2.3.3 Recent Pain Experiences Questionnaire (RPEQ)

4 items derived from the Brief Pain Inventory (Cleeland & Ryan, 1994) were used as a control measure to assess participants subjective experience of pain in the last 3 months. In accordance with Heathcote et al., (2016, 2018) and Said et al., (2019) participants reported their: i) average pain intensity and ii) worst pain intensity in the past 10 months using an 11 point Likert-type scale ranging from 0 (no pain) to 10 (worst pain possible); iii) the amount that pain had interfered with daily activities (0 – I don't miss out on any activities; 10 – I miss out on all activities); and iv) the frequency of their pain (1 - on less than 1 day each month, 6 - every day). Consistent with previous

research, a composite score was created by summing the scores across the 4 items (ranging from 1 to 36) to avoid performing multiple analyses (Heathcote et al., 2016). Higher scores represented more negative recent pain experiences.

5.2.3.4 Experimental Pain Manipulation

To experimentally manipulate pain, participants were randomly allocated to either a pain (n = 22) or no pain condition (n = 24). Those randomly allocated to the pain condition took part in the Cold Pressor Task (CPT) which involved placing their hand up to the wrist in cold water. Those randomly allocated to the no pain condition placed their hand up to the wrist in a bucket of body-temperature water. As outlined in Chapter 2 (Section 2.5.4), cold pain in the form of the CPT was selected due to its representativeness of chronic pain (i.e., unpleasantness).

5.2.3.4.1 *Cold Pressor and Warm Water Task*

A single cold-pressor unit was used (Grant Instruments, Cambridge, UK), which contains a stirred water circulator (model GR150 – S18) and refrigerated immersion cooler (Model C2G). Water was regulated at a temperature of five degrees in the cold-pressor and 37 degrees in the bucket of warm water. These temperatures were selected based upon previous research in this area (Sharpe et al., 2017). Participants in the no pain condition placed their non-dominant hand submerged to the wrist in the bucket of warm water for 240 seconds. In contrast, participants allocated to the pain condition first placed their non-dominant hand up to the wrist in the bucket of warm water for 30 seconds to control for initial wrist temperature, and then placed the same wrist in the cold-pressor.

5.2.3.4.2 *Pain Measures*

Three pain measures were recorded during the cold-pressor task for participants in the pain condition. This included, pain threshold, defined as the total time taken (in seconds) for participants to first register pain after placing their hand up to the wrist in the cold pressor; pain tolerance, defined as the amount of time (in seconds) participants kept their hand up to the wrist

submerged in the cold-pressor (for up to a maximum of 240 seconds; Maratos & Sheffield, 2020); and pain intensity, measured using a 1-item questionnaire, which asked participants to rate their current level of pain from 0 (no pain) to 10 (severe pain) on an 11-point Likert scale. Pain intensity was recorded at two intervals; when participants first registered pain (threshold) and immediately after participants withdrew their hand from the cold-pressor (tolerance), to calculate an average pain score.

5.2.3.5 Experimental Tasks

To assess whether pain influenced cognitive biases, interpretation and attentional bias tasks were presented pre and post the cold pressor/warm water task and memory bias tasks presented post and 1-month post the cold pressor/warm water task. To minimise learning effects, participants completed two versions of the same interpretation and attentional bias tasks and two different memory bias tasks (free recall and recognition). For the interpretation and attentional bias tasks, the only difference pre and post the cold pressor/warm water task were the stimuli used.

5.2.3.5.1 *Interpretation Bias Task (IBT)*

This was the IBT task developed in Chapter 3 (see also Gaffiero et al., 2022). In brief, stimuli comprised 18 ambiguous scenarios that can be interpreted in a pain/illness-related and non-pain/illness related manner. For example, "***A ball hits you in the face. You look in the mirror and see your face is covered in…"***. The scenario is ambiguous as there is a minimum of 2 different possible solutions reflecting different interpretations (e.g., Mud, Blood). 18 filler scenarios designed to have multiple non-pain/illness related associations were also included to avoid priming. For example, "***You get home from work and notice that you have left the… on".*** Again, these scenarios were ambiguous as there is a minimum of 2 different solutions but, importantly, reflecting different **non**-pain/**non**-illness-related interpretations (e.g., Light, Oven).

Task events were as follows: participants were first provided with written instructions to read the scenario and to imagine themselves in the situation; next, participants were presented with one practice trial to gain an understanding of the task requirements. Following this, each of the

ambiguous and control scenarios (in Arial, 12-point font) were presented in the centre of the computer screen in a randomised order.

For example:

'A ball hits you in the face. You look in the mirror and see your face is covered in…'

Participants were instructed to type the first word (or words) that popped into their mind to complete the scenario. This free-response format was selected to enable participants to provide their own interpretations of the scenario, as opposed to using a forced-choice response format that may not accurately reflect the participants interpretation of the scenario.

To measure interpretation biases pre and post the cold-pressor/warm water task, stimuli were randomly divided into two sets. Hence, each interpretation bias task (i.e., pre and post) contained a total of 19 non-repeated scenarios: 9 ambiguous scenarios, 9 filler scenarios, and 1 practice scenario (which was generated for the purpose of this study). The order of the interpretation bias tasks (i.e., pre and post) was counterbalanced between participants and conditions using a latin square design. To assess whether participants display IB for pain-related information an IB index was calculated. This involves subtracting the number of pain/pain-illness solutions generated from the number of non-pain/non-pain illness solutions generated. A positive score indicates an interpretation bias for pain/pain-illness related information, a neutral score (i.e., 0) indicates no evidence of an interpretation bias, while a negative score indicates an interpretation bias for non-pain/non-pain illness related information.

5.2.3.5.2 *Free viewing Attentional Bias Task*

Attentional biases were measured using a free viewing task. For the free-viewing task, stimuli were the Pain Images set developed in Chapter 4 and comprised 30 picture pairs: 10 of which contained two neutral images (neutral/neutral trial); 10 of which contained one low-pain and one neutral

image (low-pain/neutral trial), and 10 of which contained one high-pain and one neutral image (high-pain/neutral-trial). The high pain images consisted of injury-related images that possessed a high threat and high pain intensity value. The low pain images consisted of pain facial expressions and possessed a medium threat and low pain intensity value. The neutral images possessed a low threat and no pain intensity value. The properties of all images were adjusted with Microsoft Paint to achieve a uniform size. Images were presented in JPEG format and resized to 640 x 480 pixels. Due to formatting restrictions, facial expressions from the PICS (which formed the low pain intensity category), could only be resized to 640 x 512 pixels. To measure attentional biases pre and post the cold-pressor/warm water task, the stimuli were randomly divided into two sets. Each set comprised 15 image pairs (5 neutral-neutral, 5 low-pain-neutral, 5 high-pain-neutral). Additionally, the 15 image pairs were counterbalanced so that they appeared equally on the left and right size of space to create 30 trials in one block. Two blocks were presented, so that the second block was identical to the first. Prior to the commencement of both versions of the free-viewing attentional bias task, participants were presented with six practice trials. These trials comprised 1 of each stimulus pair (e.g., high-pain-neutral) that were not included in the original stimulus set, presented twice to counterbalance for location (left, right). Thus, in total, 66 trials were presented in each version of the attentional bias task, which was again also counterbalanced between participants and conditions using a Latin square design.

Experiment Builder 2.3.1. (SR Research Ltd, Mississauga, Ontario, Canada) was used to design and run the task. Trial events were as follows: participants first placed their chin on a table clamp chin cap to stabilise their head while their eye-movements were calibrated by the eye-tracker before the task started. Next task instructions were presented; participants were informed that they would first be presented with a fixation cross in the centre of the screen and were required to focus their eyes on its location. An invisible boundary trigger was created around the cross (200 x 200 box) with its minimum duration set to 500ms, meaning that participants had to maintain their gaze on the cross for 500 consecutive milliseconds to initiate stimulus presentation. If participants did not fixate on the cross within 10000ms the trial was aborted. Next, two images were presented to the left and right of the fixation cross. The centre of the left image was located at 480 x 540 pixel

and the centre of the right image was located at 1440 x 540 pixel. Image pairs were presented for a total duration of 3000ms (to measure early and later attention). Participants were asked to view the images in any manner that they wished. Upon offset of the images, participants were presented with a blank screen for 1000ms before the next trial began.

To provide a continuous measure of overt attentional deployment for the attentional bias task, an Eye Link 1000 Plus eye-tracker was used in conjunction with a 24-inch gaming monitor (ASUS VG248QE) at a pixel resolution of 1920 x 1080. This monitor was selected due to its 144hz refresh rate and 1ms response time. In accordance with previous research, a fixation was defined as an eye-position remaining within a 50-pixel area for more than 100ms (Mahmoodi-Aghdam et al., 2017). The camera to eye distance was always optimal (i.e., between 40-60cm). For analyses, areas of interest (AOIs) were created that incorporated a 50-pixel margin around each image used in the free-viewing attentional bias task. Then, consistent with AB literature, to assess whether participants displayed an AB for pain-related information, eye-tracking measures were transformed into an 'Index' using the following equation (AOI Neutral – AOI Pain) for each trial type (High-Pain-Neutral, Low-Pain-Neutral). Positive scores indicate a bias towards the AOI Pain, scores close to 0 indicate no bias, and negative scores indicate a bias towards AOI Neutral. This was calculated for indices of early attentional processing (First Fixation Proportion, Latency to First Fixation, Duration of First Fixation) and maintained attention (Total Fixation Count, Average Fixation Duration).

5.2.3.5.3 *Surprise Free Recall Task*

In this unexpected task, participants had 3 minutes to type as many words as possible (into a blank box) that they could remember using to complete any of the ambiguous scenarios in either the pre or post pain-manipulation interpretation bias tasks. The data is scored by calculating the number of pain and non-pain solutions correctly recalled separately for the pre and post pain-manipulation interpretation bias tasks, and then converting this number into a percentage.

5.2.3.5.4 *Delayed Recognition Task and Design Considerations*

This task was designed to present participants with 36 free-response words (one at a time) that they had previously used in the interpretation bias tasks. These words comprised 18 responses to ambiguous scenarios (9 in IBTv1, and 9 in IBTv2) and 18 responses to filler scenarios (9 in IBTv1, and 9 in IBTv2). In addition to these 36 (personal to the participant) words a further 36 new words were generated. These new words were individually tailored to each participant to match the number of pain/pain-illness and non-pain/non-pain illness solutions they previously used to complete the ambiguous scenarios. For example, if across both interpretation bias tasks participants interpreted 15 scenarios in a pain/pain-illness related manner and 3 scenarios in a non-pain/non-pain illness manner, they would be presented with 15 new pain/pain-illness related words and 3 new non-pain/non-pain illness words. In cases whereby participants produced duplicate responses to the Ambiguous Scenarios Task (i.e., responded to more than one scenario with an identical response), the duplicate response was excluded, and a new solution not generated. This accounted for 84 out of 1656 responses and therefore 5.07% of the data. Thus, while typically the maximum number of solutions presented was 72 (36 old solutions, 36 new solutions) in the Delayed Recognition Task, this was dependent on the number of duplicate responses for each participant (e.g., 1 duplicate response would result in 35 new and 35 old responses being presented, thus 70 in total).

The new solutions presented were individually tailored to each participant to match the number of pain/pain-illness related and non-pain/non-pain illness solutions they previously used to complete the ambiguous scenarios (18). All solutions for filler trials (18 of the 36) were also matched with a non-pain/non-pain illness solution. Importantly, all new solutions generated were designed to make sense in the context of the scenario of which the participants responses originated from. This was to enable higher ecological validity. These new words were selected from a bank of participant responses to these same scenarios during a previous validation study (Gaffiero et al., 2022, see Chapter 4) to ensure all participants received 36 new solutions, which were matched for total word length. All words were presented in Arial 12-point font.

Recognition scores were calculated using the signal detection method for pain/illness-related and non-pain/non-pain illness recognition scores including hits (responding 'Yes' to an old stimulus), misses (responding 'No' to an old stimulus), false alarms (responding 'Yes' to a new stimulus) and correct rejections (responding 'No' to a new stimulus). Correct totals were calculated by adding together the total number of hits and correct rejections, and incorrect totals calculated by adding together the total number of misses and false alarms.

5.2.4 Experimental Procedure

Following informed consent, participants were randomly allocated to the pain or no-pain condition. All participants then completed the demographic questionnaire, DASS-21 scale and the first computerised interpretation bias task. Following this, participants were asked to consent to and complete the first attentional bias task. This was requested by the ethics panel due to the graphic nature of the High Pain images used, thus participants who were blood and/or injury phobic were given the opportunity to not take part in this task. However, all participants consented to completing the AB task. Then participants took part in the pain manipulation phase (i.e. the cold-pressor or warm water task). Next, all participants completed a second interpretation and attentional bias task**.** Following this, to avoid any issues associated with the recency effect, all participants completed the RPEQ prior to the surprise free recall task. Here the instruction was to "type as many words as possible into the blank box below that you can remember using to complete ANY of the Ambiguous Scenarios presented in the Ambiguous Scenario Tasks earlier in the study". On average it took participants 1 hour and 15 minutes to complete all phases of this in-person data collection session, which was progressed in a Psychology laboratory located in the University of Derby's Kedleston Campus. 1-month post-experiment, participants were invited via email to complete a further online recognition memory task to measure the extent of memory bias over a longer retention period. Participants had been briefed about this follow-up at the end of the in-person data collection phase, but not what it entailed. This task was completed online by participants, with the instruction for them to simply select the 'Yes' or 'No' tick box option as to whether they recognised using the solution to word/s displayed to complete any of the scenarios

presented in either of the Ambiguous Scenarios Tasks one month prior. On average this task took participants 20 minutes to complete. Following completion of this online task, all participants were provided with an electronic debrief which outlined the full aims of the study and thanked participants for their time. All 46 participants completed all elements of the study (**see Figure 5.1 for Experimental Procedure Overview**).

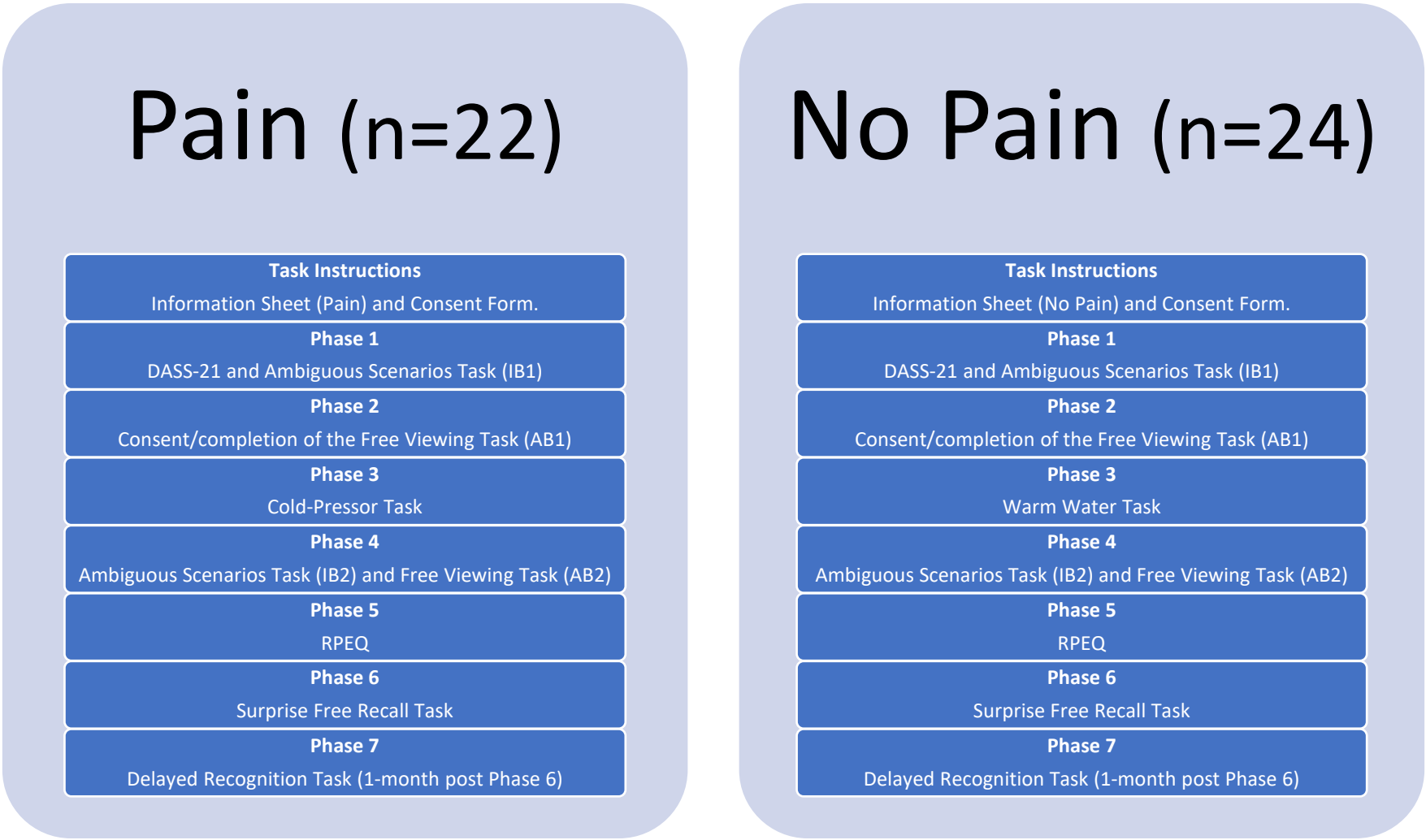


***Figure 5.1*: Experimental Procedure Overview by Pain Condition (Pain, No Pain)**

5.2.5 Data Screening

Data screening was pursued to investigate any differences in the Pain and No Pain populations in Age, Gender, Depression, Anxiety, Stress (DASS-42) and Recent Pain Experiences (RPEQ). As participants were randomly assigned, any differences occurring would reflect chance.

No significant differences in Age, Gender, Depression, Anxiety, Stress, Worst Pain, Pain Interference and Pain Frequency were observed (all $p > .05$). That said, significant between-groups differences were observed for Average Pain t (35.851) = -2.110, p = .042 (non-corrected for multiple comparisons), such that participants allocated to the pain free condition reported a higher level of average pain than their pain condition counterparts. However, the magnitude of the difference in the means (mean difference = -1.13, 95% *CI*: -2.22 to -.044) was small (eta squared = .05, Cohen, 1988, *pp*.284-7), and no other pain measure differences were significant.

Checks were also performed to examine whether there were any differences in Depression, Anxiety, Stress, Worst Pain, Pain Interference, Pain Frequency and Average Pain between participants allocated to the Pain or No Pain conditions between initial assessment and 1-month follow up (**see Table 5.1**). The ANOVA for Depression revealed a significant main effect of time $F(1,44) = 9.023$, $p = .004$, η^2 p = .170, such that depression scores were higher at the 1-month follow-up for all participants. However, no significant difference between group was observed, nor was there an interaction ($p > .05$). The ANOVA for Anxiety revealed a significant main effect of time $F(1,44) = 8.896$, $p = .005$, η^2 p = .168, such that anxiety scores were higher at the 1-month follow-up for all participants. There was no main effect of group, nor was there an interaction effect ($p > .05$). For stress, there was a significant main effect of time $F(1,44) = 4.808$, $p = .034$, η^2 p = .099, such that stress scores were higher at the 1-month follow-up for all participants. No significant difference between group was observed, nor was there an interaction ($p > .05$). For all RPEQ measures there were no significant main effects of time or group, nor were there any

interactions ($p > .05$). Thus, pain did not increase over the 4-week experimental period, nor as a consequence of randomised group assignment.

Table 5.1: Means and SDs for the DASS-42 and RPEQ by Participant Condition (Pain, No Pain) at Baseline (Time 1) and 1-Month (Time 2).

Questionnaire Indices	*Overall* Mean (SD) *Baseline*	*Acute Pain* Mean (SD) *Baseline*	*Pain Free* Mean (SD) *Baseline*	*Overall* Mean (SD) 1-Month	*Acute Pain* Mean (SD) 1-Month	*Pain Free* Mean (SD) 1-Month
Depression (DASS-42)	6.82 (5.73)	6.00 (5.82)	7.58 (5.66)	9.39 (7.42)	9.63 (7.16)	9.17 (1.59)
Anxiety (DASS-42)	8.04 (7.31)	8.18 (6.67)	7.92 (7.99)	10.61 (8.82)	7.27 (7.80)	10.50 (9.84)
Stress (DASS-42)	11.96 (8.13)	10.27 (7.67)	13.50 (8.39)	14.28 (8.34)	14.32 (7.61)	14.25 (9.12)
Pain Frequency (Last 3 months)	2.22 (1.15)	2.09 (1.11)	2.33 (1.20)	2.26 (1.16)	2.05 (1.17)	2.46 (1.14)
Pain Interference (Last 3 months)	2.33 (2.42)	1.95 (2.36)	2.66 (2.48)	2.54 (2.36)	2.18 (2.50)	2.88 (2.23)
Average Pain Intensity	2.50 (1.93)	1.91 (1.23)	3.04 (2.29)	2.48 (1.64)	2.32 (1.55)	2.63 (1.74)
Worst Pain Intensity	4.43 (2.88)	4.55 (2.97	4.33 (2.85)	4.63 (2.61)	5.13 (2.44)	4.16 (2.73)

5.3 Results

5.3.1 Exploring Interpretation Biases by Pain Condition

To investigate hypothesis 1, that participants in the pain condition would intepret more ambiguous scenarios in a pain/pain-illness related manner in the second interpretation bias task (after pain induction i.e., cold-pressor), compared to their non-pain (i.e., warm water) counterparts a 2 (Condition: Pain, No Pain) x 2 (Pain Manipulation: Pre, Post) Factorial Mixed Measures ANOVA was performed. In **Table 5.2** means and standard deviations are presented. Importantly, there was no significant main effect of Condition, such that IB index did not differ between those allocated to the pain or no pain condition $F(1, 44) = 2.605$, $p = .114$, $\eta^2 p = .056$. There was no significant main effect of Pain Manipulation, such that IB index did not significantly differ pre-or-post cold-pressor/warm water task $F(1, 44) = .030$, $p = .864$, $\eta^2 p = .001$. Lastly, there was no significant interaction between Condition and Pain Manipulation $F(1, 44) = .012$, $p = .914$, $\eta^2 p = .<.001$.

Table 5.2: Interpretation Bias Index Scores (SD) by Condition (Pain, No Pain) and Pain Manipulation (Pre/Post Cold-Pressor/Warm Water Task) for the Ambiguous Scenarios Tasks.

	Pre Cold-Pressor /Warm Water Task	Post Cold-Pressor /Warm Water Task	Total
Pain	.64 (3.47)	.82 (3.65)	.73 (3.52)
No Pain	.63 (3.88)	.67 (3.47)	.65 (3.54)
Total	.63 (3.65)	.74 (3.52)	

5.3.1.1 Summary

In sum, these results demonstrate that there were no differences between participants in the pain or no pain condition in terms of the number of ambiguous scenarios interpreted in a pain/pain-illness related manner, as a function of cold-pressor/warm water task.

5.3.2 Exploring Attentional Biases by Pain Condition

Prior to analysis, one participant from the Pain Condition was excluded due to their eye-tracking data corrupting (n = 21). To investigate hypothesis 2, that participants in the pain condition would display an AB for pain-related information presented in the second freeviewing task after pain induction (cold-pressor), compared to their non-pain (warm water) counterparts, a series of 2 (Condition: Pain, No Pain) x 2 (Pain Manipulation: Pre, Post) Factorial Mixed Measures ANOVAs were performed for each Trial Type. **See Table 5.3 for means and standard deviations below.**

Table 5.3: Mean Attentional Bias Index Scores (SD) for AB Index Measures by Condition (Pain, No Pain), Trial Type (High Pain – Neutral, Low Pain – Neutral), and Manipulation (Pre, Post Cold-pressor/Warm Water Task).

Condition	AB Index Measure	Trial Type	PRE Bias-Score	POST Bias-Score
No Pain	First Fixation Proportion	***High Pain - Neutral***	.4775 (.24772)	.3916 (.28016)
Pain	First Fixation Proportion		.3266 (.26732)	.3901 (.26586)
No Pain	Latency to First Fixation		742.0376 (398.03691)	633.0702 (405.47941)
Pain	Latency to First Fixation		591.9220 (370.58588)	632.8015 (381.32018)
No Pain	Duration of First Fixation		76.6754 (160.00680)	53.2167 (108.90914)
Pain	Duration of First Fixation		17.5233 (194.97631)	58.1147 (27.94438)
No Pain	Total Fixation Count		-2.3993 (2.27490)	-2.3313 (3.09729)
Pain	Total Fixation Count		-2.4190 (3.04953)	-2.2810 (2.78525)
No Pain	Average Fixation Duration		42.8548 (215.40888)	27.1407 (158.53911)
Pain	Average Fixation Duration		-51.0926 (220.36174)	-10.3115 (159.00395)
No Pain	First Fixation Proportion	***Low Pain - Neutral***	-.0375 (.15221)	1.030 (.22910)
Pain	First Fixation Proportion		.0316 (.15576)	.0364 (.16657)
No Pain	Latency to First Fixation		57.8494 (224.26431)	233.7877 (389.38880)
Pain	Latency to First Fixation		134.0492 (226.78298)	100.4283 (204.01255)
No Pain	Duration of First Fixation		2.6347 (108.47467)	.9948 (68.53495)
Pain	Duration of First Fixation		-37.0319 (189.00865)	-15.5916 (115.18656)
No Pain	Total Fixation Count		-.3069 (.289)	-.4000 (1.24917)
Pain	Total Fixation Count		-.6143 (1.76573)	-.5738 (1.80296)
No Pain	Average Fixation Duration		-15.9320 (90.07972)	-6.8996 (63.24089)
Pain	Average Fixation Duration		-.460532 (193.91621)	-16.2615 (85.28772)

5.3.2.1 Attentional Bias Index Scores for High Pain – Neutral Trials

No significant main effects nor interactions were observed for any of the AB Indexes. For brevity, key information is summarised in **Table 5.4** below.

Table 5.4: AB Index Measures for High Pain-Neutral Trials with Main and Interaction Effects for Condition (Pain, No Pain) and Manipulation (Pre, Post Cold Pressor/Warm Water Task).

AB Index Measure	Effect	*F*	*p*	$\eta^2 p$
First Fixation Proportion	Condition	1.627	.209	.159
	Manipulation	.046	.831	.001
	Interaction	2.051	.159	.046
Latency to First Fixation	Condition	.675	.416	.015
	Manipulation	.223	.639	.005
	Interaction	1.079	.305	.024
Duration of First Fixation	Condition	.573	.453	.013
	Manipulation	.099	.754	.002
	Interaction	1.384	.246	.031
Total Fixation Count	Condition	.000	.985	<.001
	Manipulation	.152	.698	.004
	Interaction	.018	.895	<.001
Average Fixation Duration	Condition	1.799	.187	.040
	Manipulation	.168	.668	.004
	Interaction	.947	.336	.022

5.3.2.2 Attentional Bias Index Scores for Low Pain – Neutral Trials

No significant main effects nor interactions were observed for any of the AB Indexes (see Table 5.5), except Latency to First Fixation (LFF) where an interaction effect was observed $F(1, 43) = 4.472$, $p = .040$, $\eta^2 p = .094$. Post-hoc analyses with Bonferroni correction (alpha = .0125) revealed no significant difference in LFF between the pain and no pain conditions pre cold-pressor/warm-water task ($p = .132$), or post cold-pressor/warm-water task ($p = .083$). For participants in the pain condition, no significant differences were observed in LFF pre or post cold-pressor task ($p = .300$).

However, for participants in the no pain condition differences in LFF approaching significance were observed (p = .0135, d = .48). Here, participants displayed quicker LFF for low pain images post the warm water task than pre the warm water task (p = .0135, d = .48), see **Figure 5.2**.

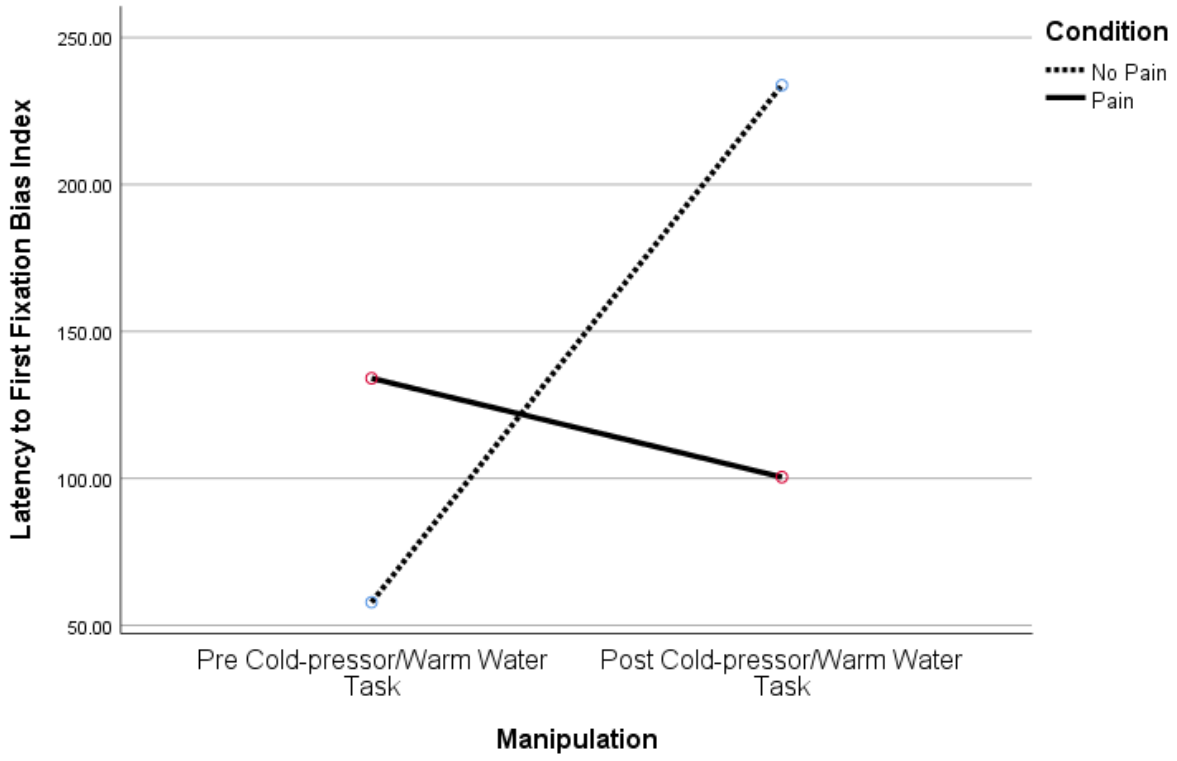


Figure 5.2: Latency to First Fixation Index for Condition and Manipulation. Positive scores indicates faster LFF for Pain, 0 indicates no bias, negative scores indicate a faster LFF for Neutral.

For brevity key information pertaining to AB Index Measures are summarised in **Table 5.5** below.

Table 5.5: AB Index Measures for Low Pain-Neutral Trials with Main and Interaction Effects for Condition (Pain, No Pain) and Manipulation (Pre, Post Cold-Pressor/Warm Water Task).

AB Index Measure	Effect	F	p	η^2 p
First Fixation Proportion	Condition	.001	.973	<.001
	Manipulation	.3575	.065	.077
	Interaction	3.124	.084	.068
Latency to First Fixation	Condition	.190	.665	.004
	Manipulation	2.062	.158	.046
	Interaction	**4.472**	**.040***	**.094**
Duration of First Fixation	Condition	.841	.364	.019
	Manipulation	.209	.650	.005
	Interaction	.841	.364	.019
Total Fixation Count	Condition	.373	.545	.003
	Manipulation	.021	.885	<.001
	Interaction	.135	.715	.009
Average Fixation Duration	Condition	.466	.499	.011
	Manipulation	.980	.328	.022
	Interaction	.280	.599	.006

5.3.2.3 Summary

To summarise, AB index scores for the High Pain - Neutral trials were all non-significant. This was consistent across AB index scores for the Low Pain - Neutral trials, except for LFF, which appeared to be driven by quicker LFF towards pain images post versus pre warm water task for participants allocated to the no pain condition.

5.3.2.4 The Effects of Stimulus Type on Indices of Early and Later Attentional Processing

To investigate hypotheses 2a/2b, that participants in the pain condition would display vigilance-avoidance for High Pain images and vigilance followed by difficulty disengaging for Low Pain images after pain manipulation compared to their No Pain condition counterparts, for each image type (high or low pain) the following analysis was conducted: Condition (No Pain, Pain) x (Image Type (High Pain, Neutral or Low Pain, Neutral) and Manipulation (Pre, Post).

Table 5.6: Eye-Tracking Measures by Condition and Manipulation.

Eye tracking Indices	Pain Condition				No Pain Condition			
	Low-Pain Neutral Trial		High-Pain Neutral Trial		Low-Pain Neutral Trial		High-Pain Neutral Trial	
	Low Pain Image	Neutral Image	High-Pain Image	Neutral Image	Low Pain Image	Neutral Image	High-Pain Image	Neutral Image
First Fixation Proportion (Pre)	.47 (.08)	.50 (.09)	.30 (.14)	.63 (.14)	.51 (.09)	.47 (.08)	.23 (.12)	.71 (.14)
Latency to First Fixation (Pre)	579.60 (149.54)	713.65 (238.20)	417.27 (111.62)	1009.19 (366.70)	615.11 (147.14)	672.96 (177.25)	336.05 (115.49)	1138.09 (346.85)
First Fixation Duration (Pre)	324.80 (173.53)	287.76 (82.28)	274.80 (148.03)	292.33 (115.67)	289.500 (107.06)	292.13 (105.83)	234.83 (38.56)	311.51 (159.92)
Total Fixation Count (Pre)	4.03 (1.34)	3.42 (1.11)	5.30 (2.10)	2.88 (1.28)	4.13 (.90)	3.82 (.82)	5.47 (1.76)	3.06 (.84)
Average Fixation Duration (Pre)	382.79 (156.48)	336.74 (123.40)	323.0 (141.39)	271.91 (137.53)	340.88 (84.61)	324.95 (79.91)	265.39 (40.25)	308.24 (199.37)
First Fixation Proportion (Post)	.45 (.10)	.49 (.11)	.26 (.14)	.65 (.15)	.44 (.12)	.54 (.12)	.27 (.12)	.66 (.17)
Latency to First Fixation (Post)	618.52 (158.49)	718.94 (174.82)	398.48 (167.26)	1031.28 (289.99)	595.19 (137.39)	828.98 (368.38)	439.96 (157.70)	398.48 (167.26)
First Fixation Duration (Post)	346.58 (167.79)	330.98 (105.64)	280.92 (139.94)	339.04 (159.24)	297.64 (102.40)	298.34 (110.81)	236.71 (36.81)	289.93 (111.61)
Total Fixation Count (Post)	3.97 (1.59)	3.40 (.81)	5.23 (2.17)	2.95 (1.07)	4.13 (.74)	3.73 (1.12)	5.56 (2.10)	3.23 (1.20)
Average Fixation Duration (Post)	364.4 (135.32)	348.14 (103.46)	312.11 (102.27)	301.80 (149.17)	337.22 (92.10)	330.33 (78.12)	261.35 (47.35)	288.49 (146.25)

5.3.2.4.1 *First Fixation Proportion*

For the High Pain images the analysis revealed a significant main effect of image type $F(1, 43) = 176.256$, $p < .001$, $\eta^2 p = .804$, such that scores were significantly higher for the Neutral AOI compared to High Pain AOI. There was no significant main effect of Manipulation $F(1, 43) = 2.296$, $p = .137$, $\eta^2 p = .051$, Condition $F(1, 43) = .640$, $p = .482$, $\eta^2 p = .015$ or an interaction (all $p > .05$). This meant that all participants were significantly more likely to fixate/visit the High Pain images first, irrespective of condition they were assigned to or time (i.e., pre vs. post manipulation).

For the Low Pain Images the analysis revealed no significant main effect of image type $F(1, 43) = .3.154$, $p = .083$, $\eta^2 p = .068$, Manipulation $F(1, 43) = 1.441$, $p = .237$, $\eta^2 p = .032$, Condition $F(1, 43) = .1.462$, $p = .233$, $\eta^2 p = .033$, nor interaction (all $p > .05$).

5.3.2.4.2 *Latency to First Fixation*

For the High Pain images a significant main effect of image type was observed $F(1, 43) = .201.704$, $p < .001$, $\eta^2 p = .824$, such that LFF were shorter for the High Pain as opposed to Neutral Images. No significant main effects of Manipulation $F(1, 43) = .026$, $p = .873$, $\eta^2 p = .001$, Condition $F(1, 43) = .1.250$, $p = .270$, $\eta^2 p = .028$ nor any interaction effects were observed (all $p > .05$). This meant that for all participants the High Pain images were able to capture participants first fixations more quickly than the Neutral images, irrespective of condition they were assigned to or time.

For the Low Pain images a significant main effect of image type was observed $F(1, 43) = 16.098$, $p < .001$, $\eta^2 p = .272$, such that a shorter LFF was observed for the Low Pain compared to Neutral images. A significant main effect of Manipulation $F(1, 43) = .8.388$, $p = .006$, $\eta^2 p = .163$ was observed, such that longer LFF were observed post compared to pre cold pressor/warm water task. No significant main effect of Condition $F(1, 43) = .213$, $p = .647$, $\eta^2 p = .005$ was observed, nor were any other interactions significant (all $p > .05$). That said, a significant Image Type x Manipulation x Condition interaction $F(1, 43) = 4.472$, $p = .040$, $\eta^2 p = .094$ was found. To simplify the data, this interaction was explored separately (split by pain condition).

A 2 (Manipulation; Pre, Post) x 2 (Stimulus Type; Low Pain, Neutral) Repeated Measures ANOVA was conducted for participants in the **No Pain Condition**. There was a significant main effect of Manipulation $F(1, 23) = .7.549$, $p = .011$, $\eta^2 p = .247$, such that LFF was longer post (as opposed to pre) warm water task. There was a significant main effect of Stimulus Type $F(1, 23) = .8.201$, $p = .009$, $\eta^2 p = .263$, such that LFF was longer for Neutral Images compared to Low Pain images. Finally, a significant Manipulation by Stimulus Type Interaction effect was observed $F(1, 23) = 5.568$, $p = .027$, $\eta^2 p = .195$.

Post-hoc analyses with Bonferroni correction (alpha = .0125) revealed no differences in LFF between the Neutral and Low Pain images pre warm water task ($p = .110$, $d = .26$). No differences were observed in LFF when comparing LFF for Low Pain images pre to post warm water task ($p = .227$, $d = .16$). However, differences were observed in LFF for Neutral images when comparing LFF pre to post warm water task ($p = .006$, $d = .56$), such that LFF was significantly longer post warm water task. Differences were also observed in LFF post warm water task ($p < .001$, $d = .60$), such that LFF was significantly shorter for Low Pain compared to Neutral images, see **Figure 5.3**.

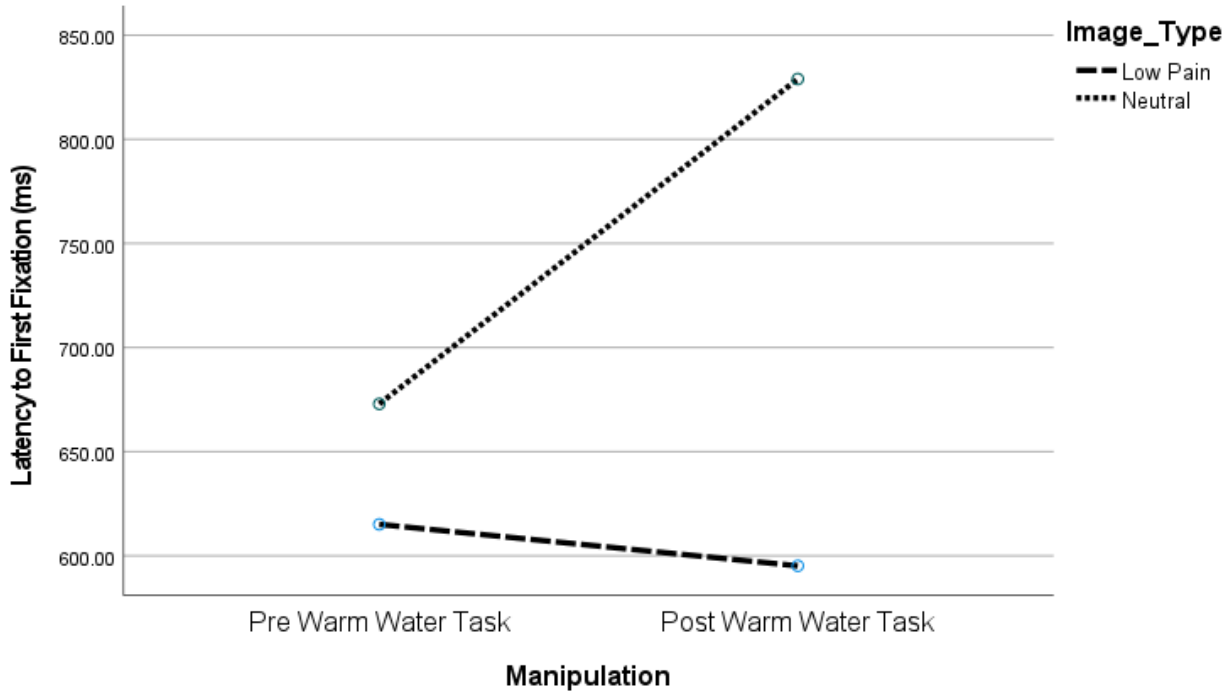


Figure 5.3: Latency to First Fixation (ms) by Manipulation (Pre, Post) and Image Type (Low Pain, Neutral) for participants in the No Pain Condition.

A 2 (Manipulation; Pre, Post) x 2 (Stimulus Type; Low Pain, Neutral) Repeated Measures ANOVA was conducted for the participants in the **Pain Condition**. There was a significant main effect of Manipulation $F(1, 20) = .7.549$, $p = .011$, $\eta^2 p = .247$, such that LFF was longer post (as opposed to pre) cold pressor task. There was no significant main effect of Stimulus Type $F(1, 20) = .1.324$, $p = .263$, $\eta^2 p = .062$. Finally, no significant Manipulation by Stimulus Type Interaction effect was observed $F(1, 20) = .286$, $p = .599$, $\eta^2 p = .014$.

These results reveal that placing one's hand in warm water resulted in a greater bias away from fixating neutral images.

5.3.2.4.3 *Duration of First Fixation*

For the High Pain images, the analysis revealed a significant main effect of image type $F(1, 43) = 8.228$, $p = .006$, $\eta^2 p = .161$, such that first fixation durations were significantly longer for Neutral as opposed to High Pain images. There was no significant main effect of Manipulation $F(1, 43) = 8.228$, $p = .513$, $\eta^2 p = .010$, or Condition $F(1, 43) = 1.238$, $p = .272$, $\eta^2 p = .028$. Furthermore, no significant interaction effects were observed (all $p > .05$). This meant that when first fixating upon each image, all participants spent less time looking at the pain images and more time looking at the neutral images, regardless of pain condition or manipulation.

For the Low Pain images, the analysis revealed no significant main effect of image type $F(1, 43) = .638$, $p = .429$, $\eta^2 p = .015$, Manipulation $F(1, 43) = 3.789$, $p = .058$, $\eta^2 p = .081$, Condition $F(1, 43) = .898$, $p = .349$, $\eta^2 p = .020$ nor any interaction effects (all $p > .05$).

5.3.2.4.4 *Total Fixation Count*

For the High Pain images, the analysis revealed a significant main effect of image type $F(1, 43) = 34.895$, $p < .001$, $\eta^2 p = .448$, such that high pain images received a higher total number of fixations than paired neutral images. There was no significant main effect of Manipulation $F(1, 43) = .765$, $p = .387$, $\eta^2 p = .017$, or Condition $F(1, 43) = 1.024$, $p = .317$, $\eta^2 p = .023$. Furthermore, no

significant interaction effects were observed (all $p > .05$). Therefore, all participants fixated more often upon the High Pain images, regardless of pain condition or manipulation.

For the Low Pain images, the analysis revealed a significant main effect of image type $F(1, 43) = 5.778$, $p = .021$, $\eta^2 p = .118$, such that low pain images received a higher total number of fixations than paired neutral images. There was no significant main effect of Manipulation $F(1, 43) = .451$, $p = .506$, $\eta^2 p = .010$, or Condition $F(1, 43) = 1.159$, $p = .288$, $\eta^2 p = .026$. Furthermore, no significant interaction effects were observed (all $p > .05$). Again, therefore, all participants fixated more often upon the Low Pain images, regardless of pain condition or manipulation.

5.3.2.4.5 *Average Fixation Duration*

For both the High and Low Pain images, no significant main effect of manipulation, condition nor interaction effects were observed (all $p > .05$).

5.3.2.4.6 Summary

Taken together, these results demonstrate that for the High Pain compared to Neutral images, participants (irrespective of condition – pain/no pain, and manipulation – pre/post), were more likely to fixate/visit the high pain images, direct their first fixation more quickly to them with the caveat of first fixations being shorter in duration, and fixate on these images more often. With respect to the Low Pain compared to Neutral Images, participants directed their first fixation more quickly to them, albeit interaction effects explored by condition revealed that participants in the No Pain condition exhibited differences in latency post-warm water task, such that latency was shorter for Low Pain images. This means that placing one's hand in warm water resulted in greater bias away from fixating neutral images. Such findings were not observed in the Pain condition. Lastly, with respect to total fixation count, a higher number of fixations were made on the Low Pain compared to Neutral images irrespective of condition.

5.3.2.5 Time Course Analysis

To further investigate hypotheses 2a/2b, dwell time, defined as the summation of the duration across all fixations on the current interest area (i.e., Pain, Neutral), the eye-tracking data was split into 6 epoch segments (1 - 0-500ms, 2 - 500-1000ms, 3 - 1000-1500ms, 4 - 1500-2000ms, 5 - 2000-2500ms, 6 - 2500ms-3000ms) for the 'High Pain – Neutral' and 'Low Pain – Neutral' Trial Types. This enabled examination as to how participants allocated to the Pain, or No Pain Condition differed in attentional allocation over the time course of stimulus presentation both pre- and post-cold-pressor/warm water manipulation.

For each trial type (High Pain – Neutral/ Low Pain - Neutral), a separate 4-way Mixed Measures ANOVA was conducted. This included one between-subjects factor: condition (pain, no pain), and three within-subjects factors: manipulation (pre-cold-pressor/warm water task, post-cold-pressor/warm water task), stimulus type (pain, neutral) and epoch (1, 2, 3, 4, 5, 6). The dependent variable was dwell time (ms).

5.3.2.5.1 *Time Course Analysis: High Pain – Neutral Trials*

The results of the four-way Mixed ANOVA for the ***High Pain – Neutral Trials*** are summarised in ***Table 5.7*** below.

Table 5.8: Test statistics of the four-way ANOVA for the effects of Condition (Pain, No Pain), Manipulation (Pre, Post), Stimulus Type (Pain, Neutral), and Epoch (1, 2, 3, 4, 5, 6).

Statistic Type	Variable Name	*F*	*p*	η_p^2
Main Effect	Manipulation	.444	.509	.01
	Stimulus Type*	**16.415**	**<.001**	**.276**
	Epoch*	**743.841**	**<.001**	**.95**
	Condition	.003	.954	<.001
Interaction	Manipulation x Condition	.465	.499	.01
	Stimulus Type x Condition	.051	.823	.001
	Epoch x Condition	.863	.507	.02
	Manipulation x Stimulus Type	.557	.460	.01
	Manipulation x Epoch*	**5.751**	**<.001**	**.12**
	Stimulus Type x Epoch*	**26.620**	**<.001**	**.38**
	Manipulation x Stimulus Type x Condition	.172	.680	.004
	Manipulation x Epoch x Condition	1.090	.367	.025
	Stimulus Type x Epoch x Condition	.245	.942	.006
	Manipulation x Stimulus Type x Epoch	.401	.848	.009
	Manipulation x Stimulus Type x Epoch x Condition	.751	.586	.017

Main effects and/or interactions in bold; p =.001, p<.001

This revealed no significant main effects of condition or manipulation. However, significant main effects of stimulus type and epoch were observed. Other notable findings included a significant interaction between manipulation and epoch, and stimulus type and epoch. All other interaction effects were non-significant ($p > .05$).

Considering no main effect or interaction effects were observed for condition (pain, no pain), analyses were re-run with condition excluded. That is, a 3-way repeated measures ANOVA was progressed for manipulation (pre, post), stimulus type (pain, neutral) and epoch (1, 2, 3, 4, 5, 6).

The results of the three-way Repeated-Measures ANOVA for the ***High Pain – Neutral Trials*** are summarised in ***Table 5.8*** below.

Table 5.8: Test statistics of the ANOVA for the effects of Manipulation (Pre, Post), Stimulus Type (Pain, Neutral), and Epoch (1, 2, 3, 4, 5, 6).

Statistic Type	Variable Name	*F*	*p*	η_p^2
Main Effect	Manipulation	.516	.012	.01
	Stimulus Type*	**16.727**	**<.001**	**.28**
	Epoch*	**747.883**	**<.001**	**.94**
Interaction	Manipulation x Stimulus Type	.528	.471	.01
	Manipulation x Epoch*	**5.619**	**<.001**	**.11**
	Stimulus Type x Epoch*	**27.139**	**<.001**	**.38**
	Manipulation x Stimulus Type * Epoch	.402	.847	.009

Main effects and/or interactions in bold; p =.001, p<.001

This revealed no significant main effects of manipulation. However, significant main effects of stimulus type and epoch were observed. Other notable findings included a significant interaction between manipulation and epoch, and stimulus type and epoch. All other interaction effects were non-significant ($p > .05$).

5.3.2.5.2 Exploring the Manipulation by Epoch Interaction for High Pain – Neutral Trials.

To explore the significant interaction between manipulation (pre, post) and epoch (1, 2, 3, 4, 5, 6) a series of paired-samples t tests were performed to compare average dwell time as a function of manipulation for each epoch. A Bonferroni-corrected alpha of $p = .016$ was adopted.

The results of the paired-samples t tests for the ***High Pain – Neutral Trials*** are summarised in ***Table 5.10*** below.

Table 5.10: Means, Standard Deviations and Test statistics comparing Dwell Time by Manipulation (Pre, Post) and Epoch (1, 2, 3, 4, 5, 6).

Manipulation	Epoch	*Mean*	*SD*		
Pre	**1**	112.60	65.01		
	2	220.65	142.65		
	3	220.12	133.06		
	4	218.97	111.95		
	5	215.06	109.18		
	6	214.66	107.43		
Post	1	108.40	67.31		
	2	218.31	142.28		
	3	220.68	119.10		
	4	219.88	102.14		
	5	220.74	107.75		
	6	220.71	113.72		
Manipulation	Epoch	***Mean Difference***	***SD***	***t***	***p***
Pre - Post	1	4.20	4.53	.927	.178
Pre - Post	2	2.33	8.41	.278	.391
Pre - Post	3	-.55	8.79	-.063	.475
Pre - Post	4	-.91	7.88	-.115	.454
Pre - Post	5	-5.67	8.67	-.654	.258
Pre - Post	6	-6.04	8.85	-.682	.249

The paired samples t-tests indicated that dwell time was not significantly different as a function of manipulation (pre, post) at epochs 1 (0ms-500ms), 2 (500ms-1000ms), 3 (1000ms-1500ms), 4 (1500ms – 2000ms), 5 (2000ms – 2500ms) and 6 (2500ms – 3000ms). A visual depiction is presented in ***Figure 5.4*** below.

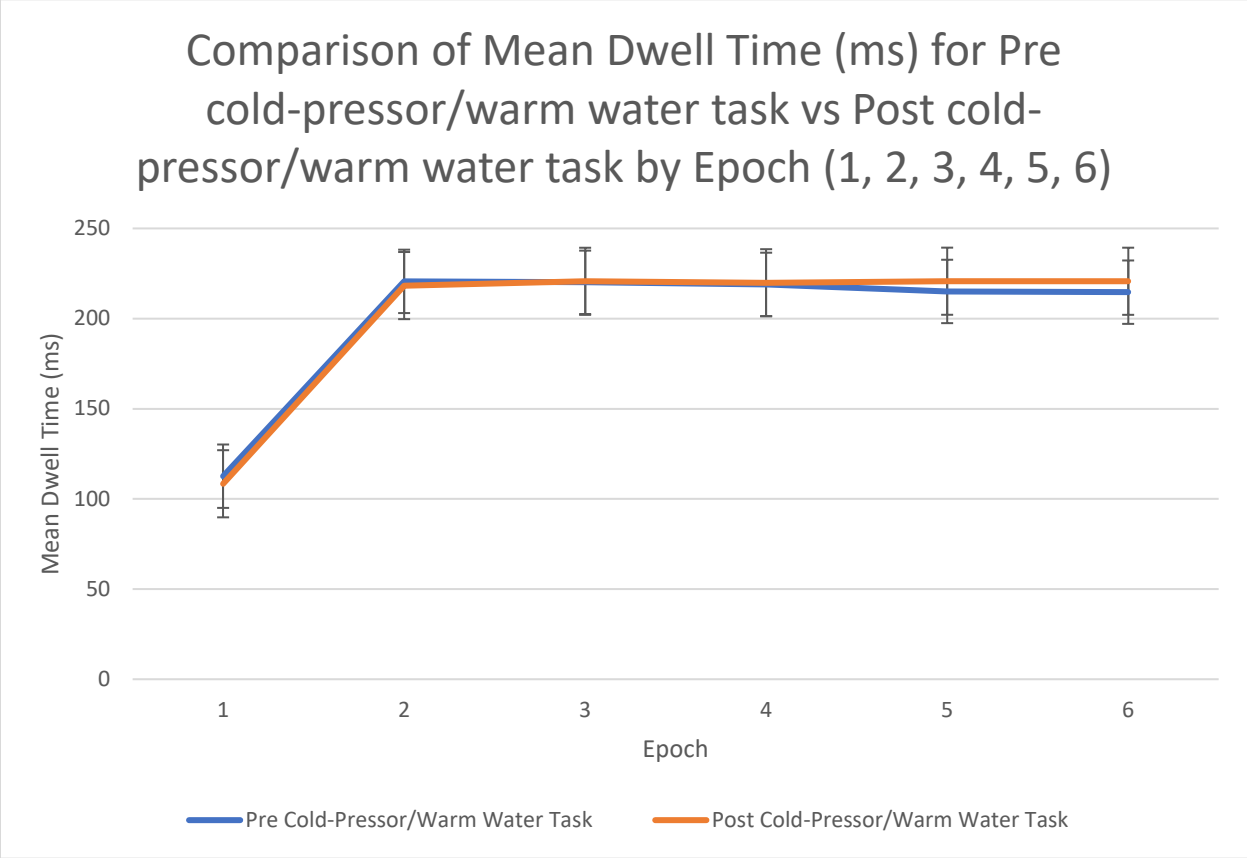


Figure 5.4: Comparison of Mean Dwell Time (ms) Pre and Post-cold-pressor/warm water task by Epoch (1, 2, 3, 4, 5, 6).

5.3.2.5.3 Exploring the Stimulus Type by Epoch Interaction for High Pain – Neutral Trials.

To explore the significant interaction between stimulus type (pain, neutral) and epoch (1, 2, 3, 4, 5, 6) a series of paired-samples t tests were performed to compare average dwell time as a function of stimulus type for each epoch. A Bonferroni-corrected alpha of $p = .016$ was adopted.

The results of the paired-samples t tests for the ***High Pain – Neutral Trials*** are summarised in ***Table 5.10*** below.

Table 5.10: Means, Standard Deviations and Test statistics comparing Dwell Time by Stimulus Type (Pain, Neutral) and Epoch (1, 2, 3, 4, 5, 6).

Stimulus Type	**Epoch**	***Mean***	***SD***		
Pain	**1**	167.04	36.66		
	2	326.25	98.10		
	3	288.38	105.08		
	4	251.18	99.82		
	5	226.73	104.81		
	6	219.59	106.50		
Neutral	1	53.96	30.92		
	2	136.52	99.55		
	3	167.63	107.99		
	4	198.30	111.07		
	5	213.99	114.96		
	6	161.20	111.47		
Stimulus Type	Epoch	***Mean Difference***	***SD***	***t***	***p***
Pain – Neutral	**1**	**113.08**	**58.61**	**18.302**	**<.001***
Pain – Neutral	**2**	**189.73**	**192.22**	**9.364**	**<.001***
Pain – Neutral	**3**	**120.75**	**208.51**	**5.494**	**<.001***
Pain – Neutral	**4**	**52.89**	**205.91**	**2.437**	**.009***
Pain – Neutral	5	12.74	216.11	.559	.29
Pain – Neutral	**6**	**58.39**	**198.69**	**2.788**	**.003***

The paired samples t-tests indicated that dwell time was significantly greater for pain compared to neutral images at epochs 1 (0ms-500ms), 2 (500ms-1000ms), 3 (1000ms-1500ms), 4 (1500ms – 2000ms) and 6 (2500ms – 3000ms). A visual depiction of these differences is presented in ***Figure 5.5*** below.

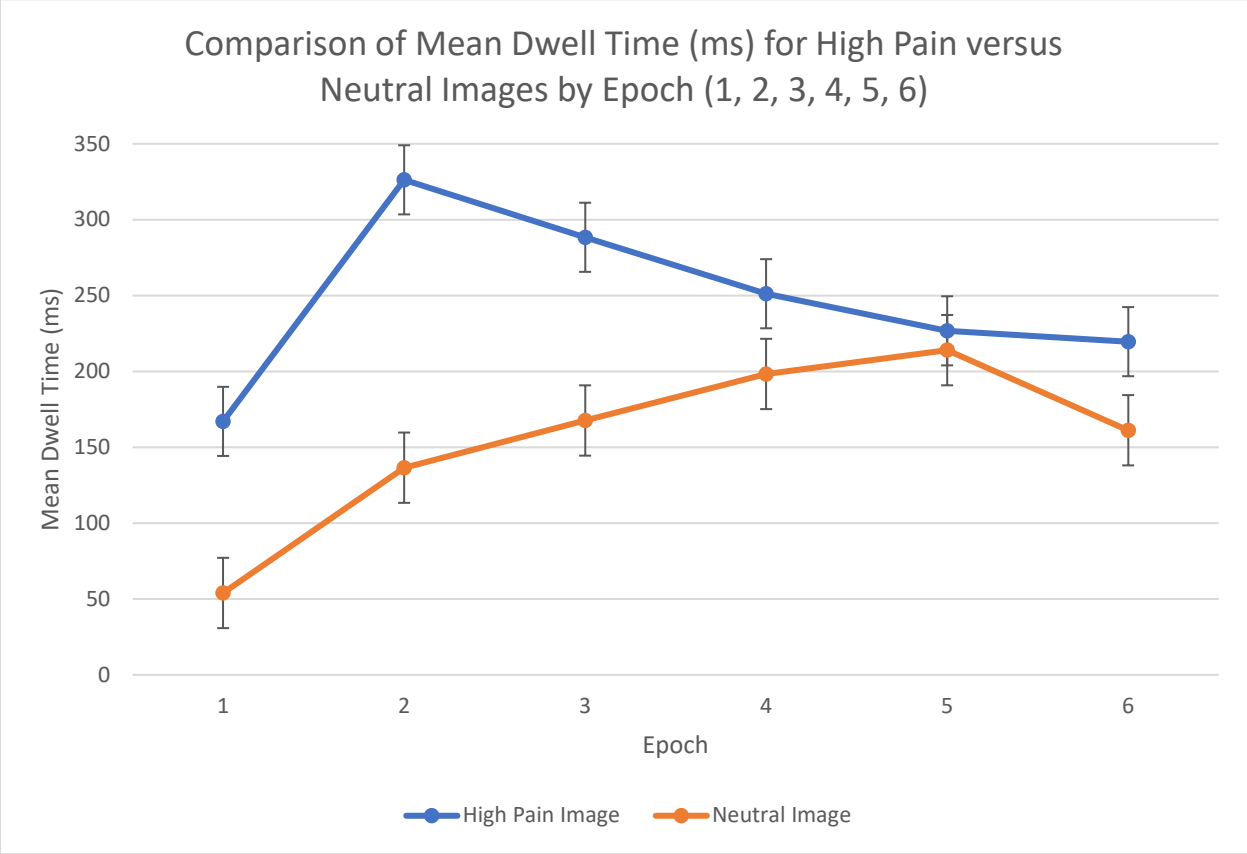


Figure 5.5: Comparison of Mean Dwell Time (ms) for High Pain versus Neutral Images by Epoch (1, 2, 3, 4, 5, 6).

5.3.2.5.4 *Time Course Analysis: Low Pain – Neutral Trials*

The results of the four-way Mixed ANOVA for the ***Low Pain – Neutral Trials*** are summarised in ***Table 5.11*** below.

Table 5.11: Test statistics of the four-way ANOVA for the effects of Condition (Pain, No Pain), Manipulation (Pre, Post), Stimulus Type (Pain, Neutral), and Epoch (1, 2, 3, 4, 5, 6).

Statistic Type	Variable Name	*F*	*p*	η_p^2
Main Effect	Manipulation	.170	.682	.004
	Stimulus Type*	**7.715**	**.008**	**.152**
	Epoch*	**753.878**	**<.001**	**.95**
	Condition	.464	.50	.01
Interaction	Manipulation x Condition	.001	.981	<.001
	Stimulus Type x Condition	.083	.775	.002
	Epoch x Condition	.946	.946	.005
	Manipulation x Stimulus Type	.166	.686	.004
	Manipulation x Epoch*	**2.354**	**.042**	**.05**
	Stimulus Type x Epoch*	**6.433**	**<.001**	**.13**
	Manipulation x Stimulus Type x Condition	.803	.375	.02
	Manipulation x Epoch x Condition	.878	.497	.02
	Stimulus Type x Epoch x Condition	.777	.567	.018
	Manipulation x Stimulus Type x Epoch	.732	.60	.017
	Manipulation x Stimulus Type x Epoch x Condition	.305	.834	.007

Main effects and/or interactions in bold = p <.001

This revealed no significant main effects of condition or manipulation. However, significant main effects of stimulus type and epoch were observed. Other notable findings included a significant

interaction between manipulation and epoch, and stimulus type and epoch. All other interaction effects were non-significant ($p > .05$).

Considering no main effect or interaction effects were observed for condition (pain, no pain), analyses were re-run with condition excluded. That is, a 3-way repeated measures ANOVA was progressed for manipulation (pre, post), stimulus type (pain, neutral) and epoch (1, 2, 3, 4, 5, 6).

The results of the three-way Repeated-Measures ANOVA for the ***Low Pain – Neutral Trials*** are summarised in ***Table 5.12*** below.

Table 5.12: Test statistics of the ANOVA for the effects of Manipulation (Pre, Post), Stimulus Type (Pain, Neutral), and Epoch (1, 2, 3, 4, 5, 6).

Statistic Type	Variable Name	*F*	*p*	η_p^2
Main Effect	Manipulation	.173	.679	.004
	Stimulus Type*	**7.805**	**.008**	**.15**
	Epoch*	**769.270**	**<.001**	**.95**
Interaction	Manipulation x Stimulus Type	.122	.729	.003
	Manipulation x Epoch*	**2.240**	**.051**	**.048**
	Stimulus Type x Epoch*	**6.753**	**<.001**	**.13**
	Manipulation x Stimulus Type * Epoch	.756	.582	.017

Main effects and/or interactions in bold; p =.001, p<.001

This revealed no significant main effects of manipulation. However, significant main effects of stimulus type and epoch were observed. Other notable findings included a borderline significant interaction between manipulation and epoch, and stimulus type and epoch. All other interaction effects were non-significant ($p > .05$).

5.3.2.5.5 Exploring the Manipulation by Epoch Interaction for Low Pain – Neutral Trials

To explore the significant interaction between manipulation (pre, post) and epoch (1, 2, 3, 4, 5, 6) a series of paired-samples t tests were performed to compare average dwell time as a function of manipulation for each epoch. A Bonferroni-corrected alpha of $p = .016$ was adopted.

The results of the paired-samples t tests for the ***Low Pain – Neutral Trials*** are summarised in ***Table 5.13*** below.

Table 5.13: Means, Standard Deviations and Test statistics comparing Dwell Time by Manipulation (Pre, Post) and Epoch (1, 2, 3, 4, 5, 6).

Manipulation	Epoch	*Mean*	*SD*		
Pre	1	118.34	24.77		
	2	217.95	69.02		
	3	218.53	87.61		
	4	219.24	69.87		
	5	213.99	67.59		
	6	212.95	69.58		
Post	1	113.99	31.56		
	2	216.32	73.75		
	3	217.82	70.60		
	4	218.26	65.50		
	5	218.26	69.17		
	6	211.79	67.48		
Manipulation	**Epoch**	***Mean Difference***	***SD***	***t***	***p***
Pre - Post	1	4.35	34.06	1.212	.115
Pre - Post	2	1.63	84.63	.183	.428
Pre - Post	3	.704	75.16	.089	.465
Pre - Post	4	.982	66.42	.140	.445
Pre - Post	5	-.426	78.33	-.516	.304
Pre - Post	6	1.161	83.17	.133	.448

The paired samples t-tests indicated that dwell time was not significantly different as a function of manipulation (pre, post) at epochs 1 (0ms-500ms), 2 (500ms-1000ms), 3 (1000ms-1500ms), 4 (1500ms – 2000ms), 5 (2000ms – 2500ms) and 6 (2500ms – 3000ms). A visual depiction is presented in ***Figure 5.6*** below.

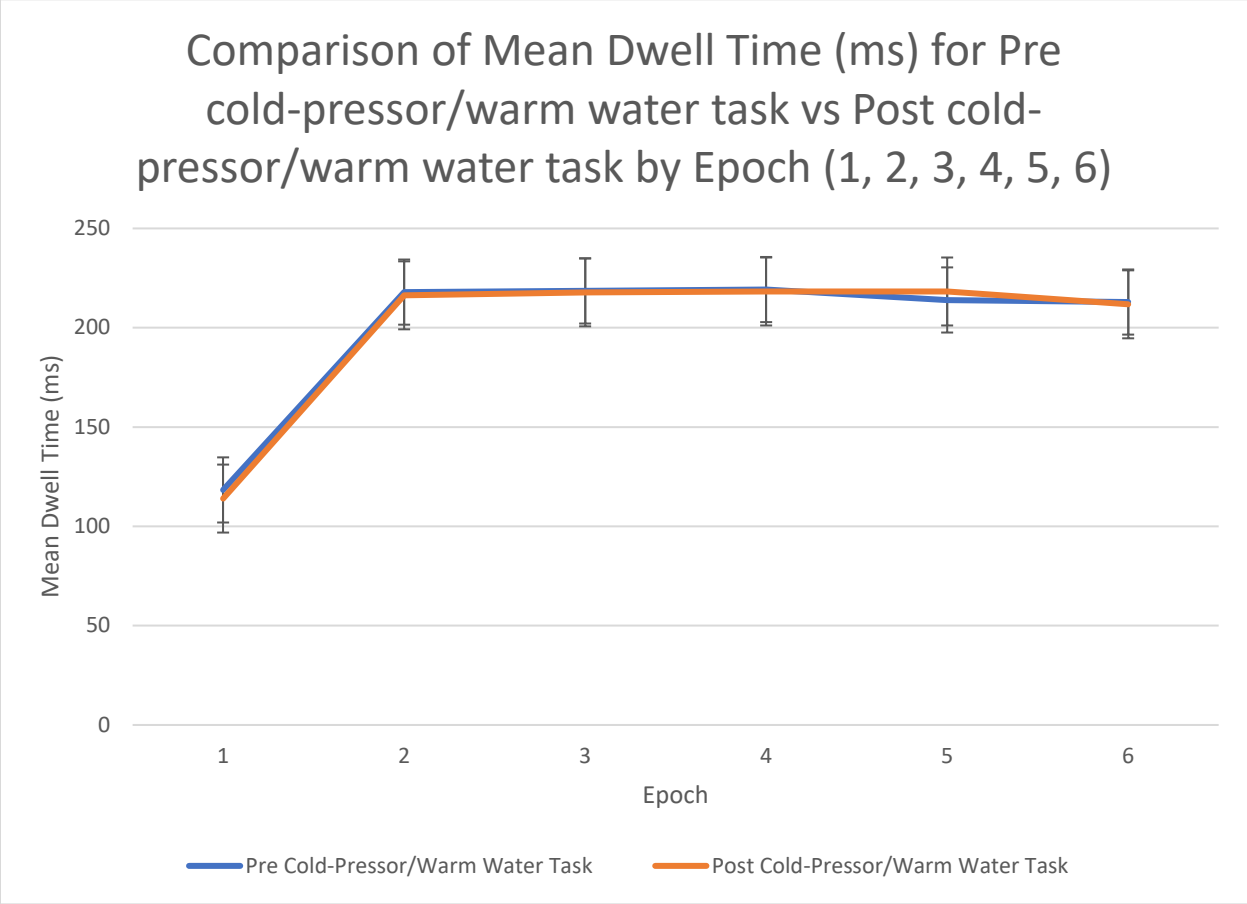


Figure 5.6: Comparison of Mean Dwell Time (ms) Pre and Post-cold-pressor/warm water task by Epoch (1, 2, 3, 4, 5, 6).

5.3.2.5.6 Exploring the Stimulus Type by Epoch Interaction for Low Pain – Neutral Trials

To explore the significant interaction between stimulus type (pain, neutral) and epoch (1, 2, 3, 4, 5, 6) a series of paired-samples t tests were performed to compare average dwell time as a function of stimulus type for each epoch. A Bonferroni-corrected alpha of $p = .016$ was adopted.

The results of the paired-samples t tests for the ***Low Pain – Neutral Trials*** are summarised in ***Table 5.14*** below.

Table 5.14: Means, Standard Deviations and Test statistics comparing Dwell Time by Stimulus Type (Pain, Neutral) and Epoch (1, 2, 3, 4, 5, 6).

Stimulus Type	Epoch	*Mean*	*SD*		
Pain	1	122.22	25.77		
	2	250.76	64.44		
	3	250.45	73.95		
	4	237.5	65.90		
	5	221.03	68.16		
	6	210.41	69.58		
Neutral	1	110.11	29.68		
	2	184.40	61.68		
	3	185.89	71.30		
	4	199.99	65.90		
	5	221.03	68.31		
	6	210.41	69.58		
Stimulus Type	**Epoch**	***Mean Difference***	***SD***	***t***	***p***
Pain – Neutral	**1**	**12.11**	**41.29**	**2.782**	**.004***
Pain – Neutral	**2**	**66.36**	**123.66**	**5.091**	**<.001***
Pain – Neutral	**3**	**64.56**	**142.66**	**4.293**	**<.001***
Pain – Neutral	**4**	**37.51**	**127.29**	**2.796**	**.003***
Pain – Neutral	5	9.81	133.43	.698	.244
Pain – Neutral	6	-3.91	133.27	-.279	.391

The paired samples t-tests indicated that dwell time was significantly greater for pain compared to neutral images at epochs 1 (0ms-500ms), 2 (500ms-1000ms), 3 (1000ms-1500ms) and 4 (1500ms – 2000ms) but not 5 or 6. A visual depiction of these differences is presented in ***Figure 5.7*** below.

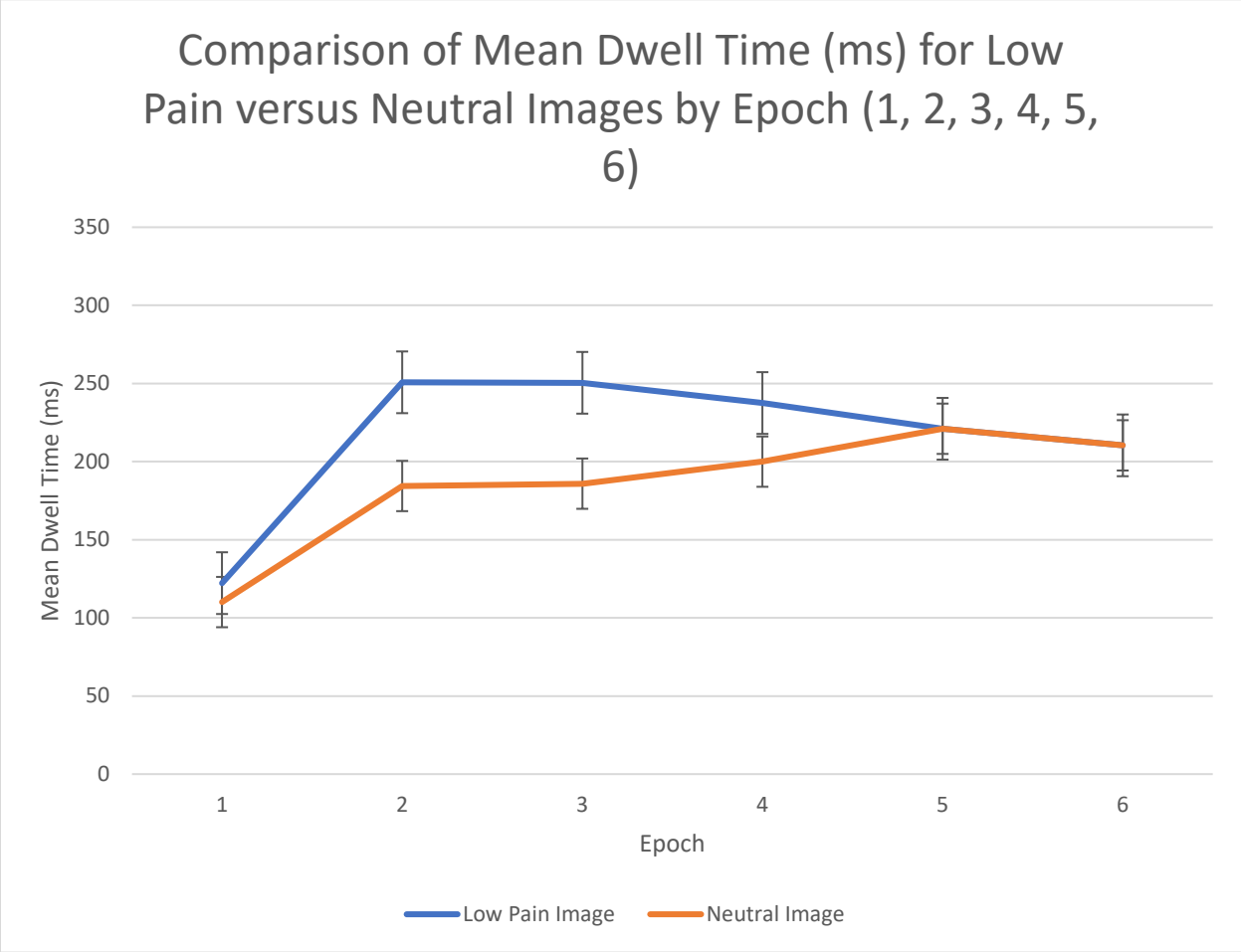


Figure 5.7: Comparison of Mean Dwell Time (ms) for Low Pain versus Neutral Images by Epoch (1, 2, 3, 4, 5, 6).

5.3.3 Exploring Recall Biases by Pain Condition

To investigate the hypothesis that participants in the Pain condition would correctly recall a higher percentage of pain/pain-illness solutions generated in the second IB task compared to their no-pain counterparts, a 2 (Condition: Pain, No Pain) x 2 (Manipulation: Pre, Post) x 2 (Free Recall Category: Pain/Pain-illness, Non-Pain/Non-Pain illness) Mixed-Measures ANOVA was performed. In **Table 5.11** means and standard deviations are presented.

Table 5.9: Mean Accuracy in Perecentage (SD) of the number of Pain/Pain-illness and Non-Pain/Non-Pain Illness Solutions correctly recalled, by Condition (No Pain, Pain) and Manipulation (Pre/Post).

		Pre Cold Pressor/Warn Water Task [First IB Task]	Post Cold Pressor/Warm Water Task [Second IB Task]	Total
No Pain Condition	**Pain/Pain-Illness**	37.75 (25.17)	39.72 (23.05)	38.74 (23.90)
	Non-Pain/Non-Pain Illness	25.44 (25.94)	22.66 (26.51)	24.05 (25.99)
	Total	31.60 (26.04)	31.19 (26.04)	
Pain Condition	**Pain/Pain-Illness**	31.17 (24.14)	38.86 (21.43)	35.02 (22.89)
	Non-Pain/Non-Pain Illness	16.86 (15.49)	42.85 (30.11)	29.85 (27.07)
	Total	24.01 (21.31)	40.85 (25.90)	

There was no significant main effect of Condition; $F(1, 44) = .090$, $p = .383$, η^2 p = .002. A significant main effect was observed for Free Recall Category; $F(1, 44) = 8.001$, $p = .007$, η^2 p = .154, such that a higher percentage of pain/pain illness solutions were correctly recalled compared to non-pain/non-pain illness solutions. Moreover, given the main effect for Manipulation was approaching statistical significance this was explored further; $F(1, 44) = .3.904$, $p = .054$, η^2 p = .082. Here, the percentage of solutions recalled post-cold-pressor/warm water task was higher compared to pre-cold-pressor/warm water task.

No interaction effects were observed between Manipulation and Free Recall Category; $F(1, 44) = 1.145$, $p = .290$, η^2 p = .025, Free Recall Category and Condition; $F(1, 44) = .1.842$, $p = .182$, η^2 p = .040, nor between Manipulation, Free Recall Category and Condition $F(1, 44) = 3.313$, $p = .076$, η^2 p = .070. That said, a significant interaction effect was observed between Manipulation and Condition; $F(1, 44) = .4.330$, $p = .044$, η^2 p = .089. Figure X provides a visual depiction of this interaction.

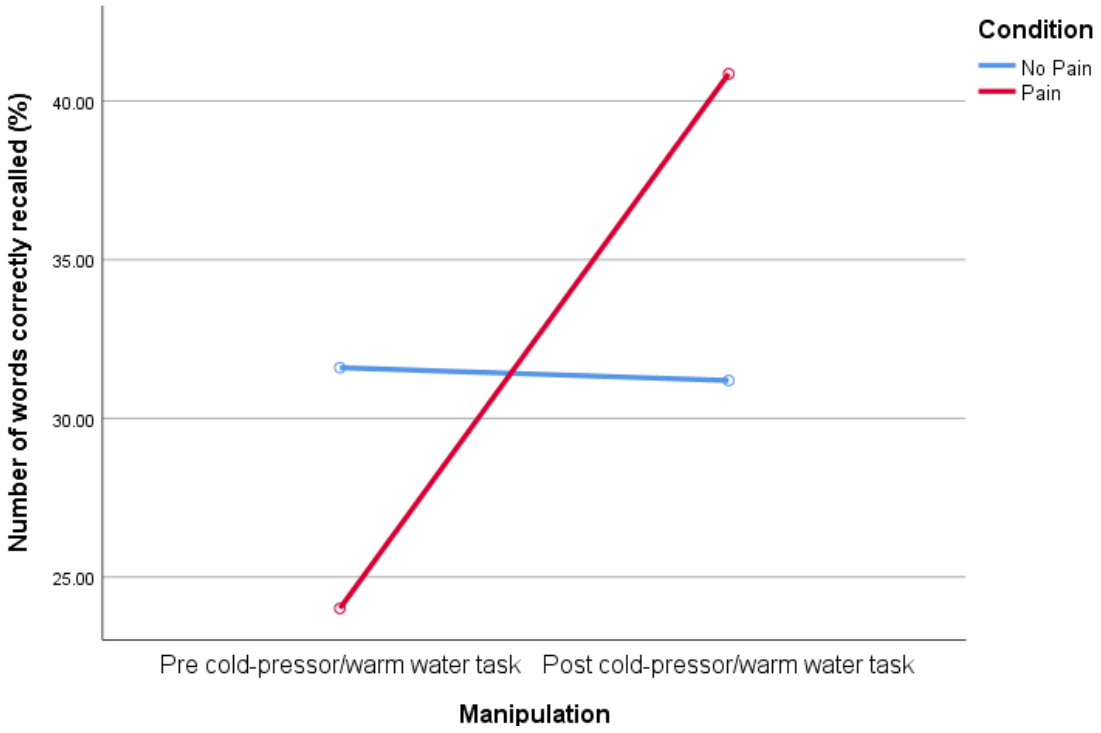


Figure 5.8: Interaction graph displaying the number of words correctly recalled (in %) by condition (pain, no pain) and manipulation (pre-cold-pressor/warm water task, post-cold-pressor/warm water task).

To explore the significant interaction between manipulation (pre, post) and condition (pain, no pain) a series of t-tests were performed to compare the number of words correctly recalled in percentage as a function of manipulation for each condition. A Bonferroni-corrected alpha of $p = .016$ was adopted.

Independent samples T-Tests revealed that there was no significant difference in the percentage of words recalled pre-cold-pressor/warm water task between the pain and no pain conditions; t = 1.520, p = .066. Moreover, no significant difference in the percentage of words recalled post-cold-pressor/warm water task was observed between the pain and no pain conditions; t = -1.782, p = .04.

Paired-Samples T-Tests revealed a significant difference in the number of words correctly recalled in percentage pre-cold-pressor versus post-cold-pressor task for participants in the pain condition; t = -.3032, p = .002. Here, the number of words correctly recalled in percentage was significantly higher post-cold pressor task (M = 40.85, SD = 25.91) than pre-cold pressor task (M = 24.01, SD = 21.31). No significant difference in the number of words correctly recalled in percentage pre warm water versus post warm water task for participants in the no pain condition was observed; t = .081, p = .468.

5.3.3.1 Summary

Considering the above, the results demonstrate that overall, participants allocated to the pain condition correctly recalled a higher percentage of solutions post-cold-pressor task. This suggests that the experience of pain enhanced recall memory irrespective of stimulus type (pain, non-pain).

5.3.4 Exploring Recognition Biases by Pain Condition

To investigate the hypothesis that participants in the pain condition would correctly recognise more pain/pain-illness related solutions 1-month later compared to their non-pain counterparts; more specifically, correctly recognise pain/pain-illness related solutions generated in the Interpretation Bias Task post pain-induction, a series of 2 (Condition, Pain, Non Pain) x 2 (Response type; Pain correct, Pain incorrect) Factorial Mixed ANOVAs were performed to examine differences in recognition between Condition and Manipulation.

5.3.4.1 Recognition Biases Pre Cold-Pressor/Warm Water Task

A 2 (Condition) x 2 (Response Type) Factorial Mixed ANOVA revealed a significant main effect of response type $F(1, 44) = 72.466$, $p < .001$, $\eta^2 p = .622$, such that there were significantly higher Pain correct than Pain incorrect responses. There was no significant main effect of condition $F(1, 44) = .915$, $p = .344$, $\eta^2 p = .020$, and no significant interaction effect $F(1, 44) = .459$, $p = .502$, $\eta^2 p = .010$ (see **Table 5.12** for Mean/SD).

Table 5.10: Mean (SD) Correct and Incorrect Recognition Scores for the Pain responses Cold-Pressor/Warm Water Task.

	Pain Correct Total	Pain Incorrect Total	Total
Pain Condition	32.72 (7.23)	17.28 (7.23)	25.00 (10.58)
No Pain Condition	33.00 (9.12)	14.91 (6.16)	23.96 (12.07)
Total	32.87 (8.18)	16.04 (6.94)	

With respect to non-pain correct and non-pain incorrect responses (see **Table 5.13** for Mean/SD), a 2 (Condition) x 2 (Response Type) Factorial Mixed ANOVA revealed a significant main effect of response type $F(1, 44) = 31.514$, $p < .001$, $\eta^2 p = 417$, such that there were significantly higher non-pain correct than non-pain incorrect responses. There was no significant main effect of condition $F(1, 44) = 1.093$, $p = .301$, $\eta^2 p = .024$. However, a significant interaction effect was observed $F(1, 44) = 4.557$, $p = .038$, $\eta^2 p = .094$ between Condition and Response Type.

Table 5.11: Mean (SD) Correct and Incorrect Recognition Scores for the Non-Pain responses Pre Cold Pressor/Warm Water Task.

	Non-Pain Correct Total	Non-Pain Incorrect Total	Total
Pain Condition	28.23 (9.86)	19.49 (8.74)	23.86 (10.22)
No Pain Condition	34.73 (9.22)	15.27 (9.22)	25.00 (13.41)
Total	31.62 (9.98)	17.29 (9.15)	

Post-hoc analyses with Bonferroni correction (alpha = .0125) were conducted to investigate the interaction between Condition and Response Type. For participants in the No Pain condition there was a significant difference in the percentage of solutions recognised between the non-pain correct and incorrect categories, such that the percentage of non-pain words correctly recognised was greater ($p < .001$, $d = 1.10$). This pattern of results was also observed for participants in the pain condition ($p < .001$, $d = .79$), such that the percentage of non-pain words correctly recognised was again greater. That said, the magnitude of the effect was greater for those in the No Pain condition (as shown by a steeper line in **Figure 5.7**). There was no difference in the percentage of non-pain words correctly recognised between participants in either of the two conditions ($p = .132$), nor was there a difference between participant conditions and the percentage of non-pain words incorrectly recognised ($p = .132$).

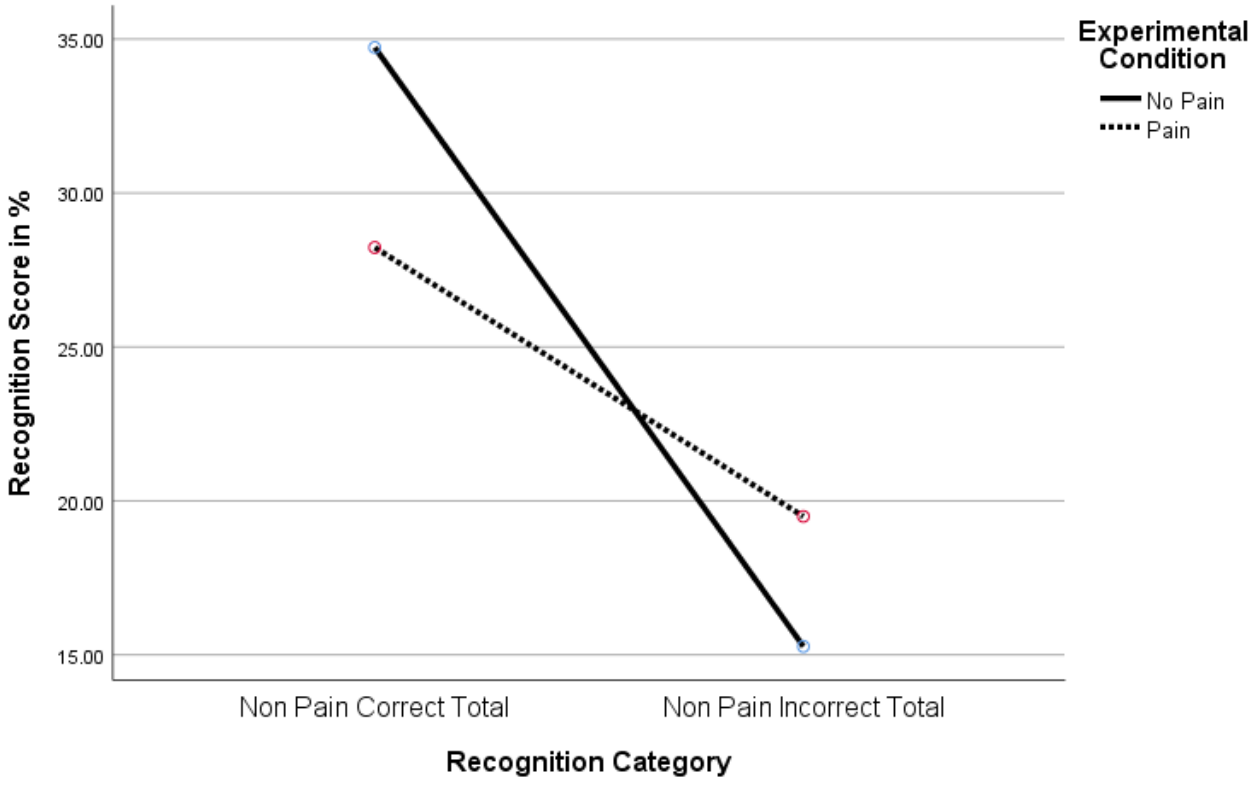


Figure 5.9: Interaction Graph for Recognition Score (%) by Condition (Pain, No Pain) for Non Pain Correct and Incorrect Totals.

5.3.4.2 Recognition Biases Post Cold Pressor/Warm Water Task

The analysis revealed a significant main effect of response type $F(1, 44) = 83.746$, $p < .001$, $\eta^2 p = .656$, such that there were significantly higher Pain correct responses than Pain incorrect responses. There was no significant main effect of condition $F(1, 44) = .1.093$, $p = .301$, $\eta^2 p = .024$, and no significant interaction effect $F(1, 44) = .411$, $p = .525$, $\eta^2 p = .009$ (see **Table 5.14** for Mean/SD).

Table 5.12: Mean (SD) Correct and Incorrect Recognition Scores for the Pain responses Post-Pain/Warm Water Manipulation.

	Pain Correct Total	Pain Incorrect Total	Total
Pain Condition	33.77 (8.79)	16.23 (8.79)	25.00 (11.89)
No Pain Condition	35.75 (6.19)	14.25 (6.13)	25.00 (12.63)
Total	34.80 (7.52)	15.20 (7.52)	

With respect to the non-pain correct and incorrect responses, the analysis revealed a significant main effect of response type $F(1, 44) = 18.111$, $p < .001$, $\eta^2 p = .292$, such that there were significantly higher non-pain correct responses than non-pain incorrect responses. There was no significant main effect of condition $F(1, 44) = 1.093$, $p = .301$, $\eta^2 p = .024$, nor a significant interaction effect $F(1, 44) = .039$, $p = .845$, $\eta^2 p < .000$ (see **Table 5.15** or Mean/SD).

Table 5.13: Mean (SD) Correct and Incorrect Recognition Scores for the Non-Pain responses Post-Pain/Warm Water Manipulation.

	Non-Pain Correct Total	Non-Pain Incorrect Total	Total
Pain Condition	29.23 (10.02)	18.50 (8.65)	23.86 (10.72)
No Pain Condition	30.88 (9.96)	19.12 (9.96)	25.00 (11.51)
Total	30.09 (9.91)	18.82 (9.26)	

5.3.4.3 Supplementary Analyses: D-Prime and Criterion C

To provide a measure of the standardised difference between the means of the signal present/absent distributions, D-prime (*d'*) was calculated for the Pain/Pain-illness and Non-Pain/Non-Pain illness recognition data Pre (pertaining to the first IB task) and post cold-pressor/warm water task (pertaining to the second IB task) using the following equation:

$$\boldsymbol{d' = \mathbf{z}(H) - \mathbf{z}(FA)}$$

Here 'z (H)' refers to the z-scores for 'Hits' and 'z (FA)' z-scores for 'False Alarms'. Larger absolute values of *d'* indicate a better ability to discriminate between a signal being present/absent and thus displaying higher accuracy on the recognition task.

Criterion C (C, also known as Response Bias) was also calculated to assess the willingness of the participants in the Pain vs. No Pain Condition to respond with a 'signal present' response during the Recognition Task. For the Pain/Pain-illness and Non-Pain/Non-Pain illness recognition data at Pre (pertaining to the first IB task) and Post Pain/Warm Water Manipulation (pertaining to the second IB task), *C* was calculated using the following equation:

$$\boldsymbol{c = -1\ \mathrm{x} \frac{\mathbf{z}(H) + \mathbf{z}\ (FA)}{2}}$$

Here 'z (H)' refers to the z-scores for 'Hits' and 'z (FA)' z-scores for 'False Alarms'. Larger absolute values of *C* indicate that participants are less willing to make a false alarm, and thus require stronger evidence before responding that a signal is present.

To examine whether there were any differences in *d'* or C between Condition and Manipulation a series of Independent Samples T Tests was performed using the Pain/Pain-illness and Non-Pain/Non-Pain illness (H and FA) scores. No significant differences were observed in *d'* or *C* Pre or Post the Cold-Pressor/Warm Water task (all $p > .05$).

5.3.4.4 Summary

To summarise, there were no between-condition differences in the number of pain/pain-illness solutions correctly recognised. Generally speaking, pre and post cold-pressor/warm water task a higher proportion of pain/pain-illness solutions were correctly (as opposed to incorrectly) recognised, and this was also observed with respect to the non-pain/non-pain illness correct recognition data. However, condition did affect recall for words in the pre cold-pressor/warm water task IB task. Here, whilst participants in both groups exhibited a higher proportion of non-pain correct than incorrect responses, the magnitude of the effect was greater for participants in the No Pain condition. So, being subjected to warm-water, to some extent, influenced recall of non-pain words presented prior to the warm-water experience. Lastly, no differences in ***d'*** or *C* were observed.

5.3.5 Investigating the Relationship between Cognitive Biases and Pain Outcomes.

Finally, to investigate hypothesis 5, that relationships would emerge between cognitive biases and pain outcomes for participants allocated to the Pain condition a series of bivariate correlations were conducted for indices of Interpretation, Attention and Memory (Recall and Recognition) bias with respect to pain threshold, tolerance and average pain. Pain threshold, tolerance and average pain were not found to correlate with any indices of Interpretation, Attention or Memory (Recall and Recognition) pre-CPT (all $p > .05$). Post-CPT significant correlations emerged across each of these biases. For brevity, only significant correlations are reported below.

5.3.5.1 Pain Threshold

Significant negative correlations were observed between; pain threshold and the number of scenarios interpreted in a pain/pain-illness manner during the second Interpretation Bias task (r = -.567, p = .007): pain threshold and the number of pain words correctly recalled from the second Interpretation Bias task (r = -.475, p = .03), and pain threshold and the number of pain words correctly recognised 1-month later (r = -.572, p = .007). These findings indicate that as the time

taken to first report pain decreases, interpretation, recall and recognition of pain/pain-illness words all increase. With respect to Attentional bias, a positive relationship was only observed between pain threshold and total fixation count for the High Pain (r = .490, p = .024) and Low Pain images (r = .623, p = .003), indicating that as time taken to first report pain increased so too did total fixation count for these images.

5.3.5.2 Pain Tolerance

With respect to pain tolerance, a significant negative correlation was observed between pain tolerance and the number of scenarios interpreted in a pain/pain-illness manner during the second Interpretation Bias task (r = -.465, p = .034), and pain tolerance and first fixation proportion for High Pain images (r = -.440, p = .046). This indicated that the quicker participants removed their hand from the cold-pressor the more ambiguous scenarios were interpreted in a pain/pain-illness manner and that first fixations were more likely to be directed towards the High Pain images in the second AB task.

5.3.5.3 Average Pain

No significant correlations emerged between Average Pain and any indices of Interpretation, Attention or Memory (Recall and Recognition) Bias (all p > .05) post CPT.

5.3.5.4 Summary

To summarise, the above findings indicate that average pain did not correlate with any cognitive bias. However, pain threshold was negatively correlated with Interpretation, Recall, Recognition and Total Fixation Count (for High and Low Pain images), and pain tolerance was negatively correlated with Interpretation and First Fixation Proportion for High Pain images. These findings suggest that participants who are more sensitive to pain (i.e., quicker to first report pain, quicker to remove their wrist from the CPT) exhibit greater biases towards pain/pain-illness relevant stimuli following a painful experience.

5.4 Discussion

The aim of this study was to measure attention, interpretation, and memory biases pre and post a pain (cold-pressor) or no pain (warm water task) situation to investigate if being subjected to acute pain influences cognitive biases. With respect to IB, no significant between-condition differences nor condition by manipulation interactions in the number of ambiguous scenarios interpreted in a pain/pain-illness manner were observed. Thus, in respect to hypothesis 1, no differences were observed between participants in the pain or no pain condition with respect to the number of scenarios interpreted in a pain/pain-illness manner, as a function of cold-pressor/warm water task. As such there was a failure to reject the null hypothesis.

With respect to AB, an interaction effect for latency to first fixation (LFF) index was observed as a function of Low Pain vs. Neutral trials and participant condition (pain, no pain). This indicated that for participants in the no-pain (warm water) condition, LFF for Low Pain images decreased post warm water task as compared to pre the warm water task. No other notable condition differences and/or interactions were observed for the other AB index analyses. Hence, hypothesis 2 that participants in the acute pain group would display an AB to pain-related information post-pain induction was not supported. Here, again, there was a failure to reject the null hypothesis. That said, during High Pain – Neutral trials, participants in both the pain and no pain condition were more likely to direct their first fixation towards High Pain images and the latency to first fixation was shorter for High Pain images, indicating biases in early attention toward pain for all participants.

Additionally, with respect to sustained attention, duration of first fixation was significantly shorter for High Pain images, albeit these images possessed a higher total fixation count also indicating biases in sustained attention. Time course analyses demonstrated significant differences in dwell time favouring High Pain images during Epochs 1-4 and 6, indicating attentional biases towards pain in the early and later-phases of attentional processing, specifically initial vigilance followed by difficulty disengaging. Similar findings were also observed for Low Pain – Neutral trials, namely latency to first fixation was shorter for Low Pain images, and these images received a higher total number of fixations (as compared to neutral images). Dwell time was also

significantly greater for these images during Epochs 1 and 4, again indicating biases during the early and middle-phases of attentional processing. Although as no differences were observed during Epochs 5 and 6, this indicates disengagement from low pain images (cf. high pain images) during the later stages of attentional processing. Overall, while there was a failure to reject the null hypothesis for hypotheses 2a/2b, these findings provide evidence to suggest AB towards pain-related information is ubiquitous and independent of condition (pain, no pain) and manipulation (pre, post).

In relation to memory biases, recall bias analyses revealed a significant interaction between condition and manipulation indicating that participants in the Pain condition correctly recalled a higher percentage of solutions post cold-pressor task. This suggests that the experience of pain enhanced recall for both pain and non-pain words. Therefore, hypothesis 3 that participants in the Pain Condition would recall more pain/pain-illness related solutions post-pain induction was partially supported. With regards to recognition memory, measured at one-month post the experimental session, while participants obtained a higher pain correct than pain incorrect percentage and higher non-pain correct than non-pain incorrect percentage both pre and post cold-pressor/warm water task, no between-condition differences were observed. That said, a significant interaction was observed between condition and response type pre cold-pressor/warm water task. This effect reflected that while participants in both conditions obtained a higher non-pain correct percentage (reflecting more non-pain words were recognised), the magnitude of the effect was higher for those in the no pain condition. Thus, in respect to hypothesis 4, participants in the pain condition did not significantly recognise more pain/pain-illness related solutions one-month later compared to their no pain counterparts, as such there was a failure to reject the null hypothesis.. Supplementary analyses revealed no differences in D-Prime or Criterion C with respect to recognition bias.

Lastly, Hypothesis 5, that relationships would emerge between AB, IB MB, and pain outcomes post-pain induction for participants in the pain condition, was partially supported. To expand, no significant correlations were observed between cognitive biases and cold-pressor data pre cold-pressor task, as expected. However, significant relationships emerged post cold-pressor

task. Pain threshold negatively correlated with IB, Recall and Recognition for pain/pain illness solutions, and positively correlated with Total Fixation Count for both High and Low Pain images. Pain tolerance negatively correlated with IB for pain/pain-illness solutions and First Fixation Proportion for High Pain images, while Average Pain did not correlate with any indices of cognitive bias. Taken together, these findings provide some evidence to suggest that a single experience of pain can influence cognitive biases, but this would appear dependent on pre-existing pain sensitivity. These findings are not surprising, given that attenuated attending to one stimulus over another will result in attenuated encoding, and thus (likely) attenuated memory recall and recognition.

5.4.1.1 Effects of Acute Pain on Interpretation Bias

Previous research indicates that youth and adults with chronic pain display a negative interpretation bias favouring pain-related information (Heathcote et al., 2016, 2017; Lau et al., 2019; Schoth et al., 2018, 2019; Chan et al., 2020). It is argued that interpreting pain as harmful and threatening induces pain-related fear, causing individuals to become hypervigilant to pain (Todd et al., 2018). However, the findings of the current study did not accord with this research indicating that a single acute pain experience is not suffficent to bias IB sufficiently towards pain to observe between-condition differences. The extent to which a single acute pain experience can bias interpretation towards negative (i.e., pain-related) information in a sample of healthy participants has only been examined once before (Todd et al., 2016). In this previous research it was found that threat and pain manipulation did not affect interpetation biases. In brief, Todd et al. (2016) recruited a sample of healthy participants and manipulated threat by providing participants with threatening or reassuring information regarding an upcoming Cold-pressor Task. They measured IB using the Incidental Learning Task which involved presenting a facial expression (happy, painful), which then was subsequently superceeded by a letter (‘H’) that would appear on the left or the right of the screen. The type of facial expression presented detemined which side the letter appeared (happy faces – target left, painful faces – target right). Participants were asked to left click on a mouse if the ‘H’ appeared on the left, and right click on a mouse if the ‘H’ appeared on the right. Results indicated no significant differences in the time taken to

identify the target appearing in the former location associated with the painful and/or happy facial expressions, and no interaction between threat and ambiguity resolution. These results indicate that threat was not sufficient to bias interpertation towards pain-related facial expressions. Moreover, IBs were found not to be associated with pain outcomes. As such the authors argued that IB, as measured by the Incidental Learning Task, may not be relevant to the experience of pain in healthy samples. Our results are in agreement with this assertion, and importantly demonstrate a similar effect using a different IB task, where care was taken not to bias participant responding.

To expand, the present study utilised the Ambiguous Scenarios Task. While this marks the first time this task has been used to measure IB before and after a pain-or-no-pain-situation in a healthy adult sample, these scenarios were previously validated by the author (Gaffiero et al., 2022; see Chapter 3) in a healthy adult sample. In this prior research, it was found that adults reporting more recent pain experiences were significantly more likely to endorse using pain-related solutions to complete ambiguous scenarios. As stated above, therefore, one explanation for the null finding in this present study is that one single instance of pain is not sufficient to induce interpretation biases in healthy pain-free adults. This is also consistent with finding that pain-related IBs are larger in individuals with chronic pain as opposed to healthy individuals (Schoth & Liossi, 2016).

This stated, it is important to note that while Todd et al. (2016) found IBs were not associated with pain outcomes, the findings of the present study revealed that IBs (measured post cold-pressor task) shared a negative relationship with pain threshold and tolerance. To expand, when considering participants in the pain condition only, those participants who reported pain more quickly and/or removed their hand from the cold-pressor task more quickly were significantly more likely to interpret the ambiguous scenarios in a pain/pain-illness manner. In explanation of these correlational findings, it may be that for participants with relatively low pain thresholds/tolerances a single instance of pain is sufficient to influence interpretation for pain. However, for those with higher pain thresholds/tolerances, this single instance is not potent enough to mediate/moderate cognitive biases. Therefore, ensuring that pain sensitivity is included in any

future IB studies is arguably extremely important in understanding how this additional factor may subsequently influence pain-related cognitive biases.

5.4.1.2 Effects of Acute Pain on Attentional Bias

A recently published systematic review of the AB and pain eye-tracking literature found biases indicative of vigilance and avoidance to be ubiquitous and not influenced by current pain status (Blaisdale-Jones et al., 2021). Such findings contradict previous systematic reviews (e.g., Todd et al., 2018) that concluded ABs to be specific for sensory-pain words amongst chronic pain populations. In an attempt to explain this contradiction, Blaisdale-Jones et al. (2021) posited that advancements in stimulus selection (i.e., selection of pictorial stimuli which are more ecologically valid than word stimuli), and paradigm choice (i.e., selection of free-viewing tasks which are more naturalistic) may explain the universality of ABs being observed (or otherwise). In the present study, validated pain-related pictorial stimuli were carefully selected and organised into two different trial types; a high-pain vs. neutral trial type, which involved pairing a pain image with a 'high pain intensity and high threat value' with a neutral image; and a low-pain vs. neutral trial type, which involved pairing a pain image with a 'low pain intensity and medium threat value' with a neutral image. These trial types were then presented using a free-viewing paradigm. The findings of the present study accord with the proposals of Blaisdale-Jones et al. (2021). That is, significant differences (i.e. main effects) were observed in AB analyses when 'stimulus category' (high or low pain vs. neutral) was included as a variable, indicating that participants (irrespective of pain manipulation) displayed an AB towards the pain-related stimuli.

To expand, with respect to the High Pain vs Neutral trials ***all participants*** fixated on the High Pain images first, displayed a faster time to first fixation with the duration of first fixation being shorter, and fixated upon these images more often, regardless of pain manipulation IV. With respect to the Low Pain vs Neutral trials ***all participants*** were found to display a faster time to first fixation and fixated upon the Low Pain images more often, again regardless of the pain maniplation IV. Taken together, these findings add credence to the notion that ABs to pain-related information are ubiquitous in accord with Blaisdale-Jones et al. (2021). In the research of Blaisdale-Jones et al. (2021) cognitive biases in chronic pain and healthy control participants were investigated.

Findings revealed that that while participants demonstrated AB on some indices during early and late attention, no between-groups differences were observed. They explained this finding as reflecting pain capturing and then holding attention as an adaptive response, as generally one needs to quickly identify pain and protect the injured area to prevent further damage. This accords with Motivational relevance theory (Maratos & Pessoa, 2019). Developed from a review of literature and findings of how emotion influences attentional biases, this theory asserts that various factors determine attentional prioritisation of different stimuli. These factors include stimulus saliency, task demands, cognitive and emotional states, which influence potential relevance of a stimulus to an individual. Applying the key tenets of Motivational relevance theory to Pain, all individuals should exhibit a bias for processing pain-related information given pain is relevant to all individuals to attend to (as it reflects the threat of harm). Thus, all individuals should display attentional biases and prioritisation of painful stimuli as these biases then allow an individual to generate a potentially protective response in situations whereby bodily harm is a possibility. Interestingly, Motivational relevance theory shares similarities with the Integrated Functional Contextual Framework (Van Ryckeghem et al., 2019), such that cognitive biases, including Attention, are not viewed as inherently maladaptive. Instead, it is the context within which these cognitive biases occur that determine their adaptive value and impact on an individual.

The Threat Interpretation Model (Todd et al., 2015) proposes that AB is dependent on the interpretation of a stimulus as being both pain-related and threatening, and that AB changes over the course of stimulus presentation. More specifically, if a stimulus is percieved to be threatening a vigilance-avoidance pattern of processing ensues. That said, the level of threat is also important; under conditions of sustained attention the TIM posits that low threat leads to easy disengagement of attention, moderate threat to more difficulty disengaging attention, and high threat to attentional avoidance. Consistent with this notion, the present study found evidence of all participants displaying biases during initial orienting, with high pain images being the first to be fixated upon more often and the time to first fixation being significantly shorter, providing evidence of vigilance towards the high pain images. With respect to sustained attention, duration of first fixation was significantly shorter for high pain images and the high pain images received a significantly higher total number of fixations. Time course analyses revealed significant differences in dwell time for

the high pain images for epochs 1-4 and 6, with dwell time significantly higher for high pain images. These findings demonstrate initial vigilance and continued capture of attention by the high pain images, which possess both a high threat and pain intensity value. This suggests that the high pain images were favoured during the early and middle stages of attention irrespective of manipulation (pre or post cold-pressor/warm water task).

With respect to the low pain images, LFF was significantly shorter compared to the paired neutral images, and overall the low pain images received a higher total number of fixations. That said, no differences were observed for first fixation proportion, duration of first fixation or average fixation duration. Time course analyses revealed significant differences in dwell time for the low pain images for epochs 1-5, but not epochs 5 or 6. These findings demonstrate initial engagement during early attention followed by disengagement from low pain images during later attention.

Considering the above, these findings partially support the TIM. To expand, while there was clear evidence of initial vigilance for the High Pain Images, it was expected that avoidance would have been observed during the later stages of attention given these stimuli possess a high threat value. So this later stage findings is not consistent with the TIM. Comparitively, for the Low Pain images, which possess a medium threat value, there was some evidence of initial vigilance and then disengagement. This finding may be explained by the stimuli for the low-pain trial type comprising facial expressions. Upon initial presentation, enhanced attentional allocation (i.e., vigilance) may be warranted to decode the facial expressions (of which humans are evolutionary equipped to do so rapidly), however, once encoded the percieved threat value may decrease resulting in disengagement from these stimuli during the later stages of attentional processing, which would explain the drop in significance in dwell time from Epochs 4 to 6, supporting the TIM.

Why results did not reveal high threat was avoided could reflect that the high-pain images included photographs of injuries, which have been postulated to require more in-depth semantic processing (Priebe et al., 2021) Additionally, if all individuals attend to what is most relevant (Maratos and Pessoa, 2019), in the context of the present study high pain images would be the most relevant, low pain images would be less relevant (but still capture attention), and neutral

images least relevant. Therefore, high pain images should receive the greatest attentional prioritisation, low pain images a degree of attentional prioritisation and neutral images the least/minimal attentional prioritisation. Hypotheses that fit with the dwell times observed for the time-course data as a function of trial type (i.e., high-pan, low-pain, neutral).

Taken together, the above findings indicate that ABs to pain-related information are ubiquitous and not influenced by pain manipulation, corroborrating the findings of a recent systematic review of the AB and pain eye-tracking literature (Blaisdale-Jones et al., 2021). The manipulation of threat via stimulus selection in context of the current study lends some support to the TIM, particularly in relation to initial vigilance. More generally, these findings support an evolutionary account of AB, which holds the view that attentional biases for pain-related information are ubiquitous given that it confers a survival advantage allowing us to detect and respond to potentially dangerous situations (Maratos and Pessoa, 2019) that may inflict bodily-harm.

It must be noted, however, that suprising findings of the current study were that when analysing the AB data a number of interaction effects were observed to be driven by the No Pain condition. To expand, AB Index analyses for latency of first fixation (LFF) revealed that participants in the No Pain condition exhibited faster LFF towards the Low Pain images post warm-water task. These findings indicate that following a potentially pleasant experience (i.e., warm water task), participants in the No Pain conditon exhibited enhanced attentional allocation to pain-related information (pain facial expressions). This is surprising, but in considering the implications of these findings the research of Lautenbacher et al. (2010) may be relevant. To recap, patients with high pain intensity at three and six-months post-surgery displayed an attentional bias for positive words in a dot-probe task completed 1 day prior to surgery. Here it was argued that avoiding the necessary confrontation of pain may increase the likelihood that these individuals will develop chronic post-operative pain. The findings of the present study suggest that a potentially pleasurable experience increases attentional allocation towards pain-related facial expressions. Thus, a future line of research enquiry might reflect if providing participants with a

pleasurable experience before exposure to pain enables individuals to cope with pain. Certainly, this seems to be a finding of some recent research (e.g., Maratos and Sheffield, 2021).

With respect to the correlational analyses examining the relationship between AB indices and pain outcomes for participants in the Pain condition, no correlations were observed pre cold-pressor task as expected. Post cold-pressor task, however, as pain threshold increased so too did total fixation duration for high and low pain images, and as pain tolerance decreased first fixation proportion for high pain images increased. This latter finding contradicts previous research by Todd et al. (2016) who found that a greater proportion of first fixations on affective pain stimuli was positively correlated with pain tolerance. However, it is consistent with The Integrated Functional Contextual Framework (IFCF, Van Ryckeghem et al., 2019). To recap, in this theory, it is proposed that along with inflexbility in interpreting and remembering pain-related information, inflexibility in the way individuals attend to such information results in negative pain outcomes.

5.4.1.3 Effects of Acute Pain on Memory Bias

The present study measured both recall and recognition biases.

5.4.1.3.1 Effects of Acute Pain on Recall Biases

In respect to recall bias, participants in the pain condition correctly recalled a higher proportion of solutions post (as opposed to pre) cold-pressor task. This implies that an acute pain experience enhances immediate recall for pain and non-pain related words. This result was unexpected, especially considering it was hypothesised that participants allocated to the pain condition would correctly recall a higher percentage of pain solutions post cold-pressor task only.

Whilst this finding was unexpected, one explanation is that within the more broader emotion literature emotion has been demonstrated to strengthen high-priority memory traces and weaken low priority memory traces (Sakaki et al., 2014). According to this logic, following the cold-pressor task, participants in the pain condition may have assigned the ambiguous scenarios presented in the second IBT as more relevant and thus of a higher priority. Consequently, the

solutions generated to each scenario (irrespective of whether they were pain-related or non-pain related) were more likely to be encoded and subsequently recalled, which offers one potential explanation as to how an acute pain experience (i.e., cold-pressor) can enhance/bias (immediate) recall, such that a higher proportion of the solutions generated in an IB task following the aformentioned pain experience, are recalled.

Despite the above evidence providing partial support for hypothesis 3, mixed findings have been a common theme amongst recall memory bias research. A recent systematic review of the recall bias literature by Schoth et al. (2020) synthesised the evidence for pain-related recall biases in individuals with chronic pain stating the current evidence is inconclusive. The extent to which this is due to methodological hetereogeneity in studies measuring recall bias (e.g., task design; expected/unexpected, task instructions) remains to be established, but at present it appears difficult to draw conclusions from the current literature. This stated, previous studies by Schoth et al. (2018, 2019) measured MB in a sample of individuals with Chronic Headache utilising the same paradigm and stimuli and found evidence of a recall bias favouring sensory-pain/disability words in one study (Schoth et al., 2018), but no between-groups differences for recall bias in the other (Schoth et al., 2019). Thus, even with consistency in population, paradigm/stimulus selection and task instructions, contradictory findings emerge. Considering this, more research is needed in both acute and chronic pain samples to attempt to disentangle the conflicting findings. Indeed, with respect to individuals suffering with acute pain more generally, given that repeated experience of pain is important, more longditudinal studies measuring recall biases may be an interesting avenue of future research.

Finally, correlational analyses between recall bias and pain outcomes revealed a negative relationship between pain threshold and the number of pain/pain-illness words correctly recalled post cold-pressor task for participants in the Pain condition. This supports the previous line of argument relating to pain sensitivity. Individuals more sensitive to pain (i.e., report experiencing pain more quickly) were more likely to recall pain/pain-illness related solutions used to complete the ambiguous scenarios post cold-pressor task.

5.4.1.3.2 Effects of Acute Pain on Recognition Biases

With respect to recognition bias 1 month later, again, no significant differences between the Pain and No Pain conditions were observed. That said, participants generally obtained a higher percentage of pain correct than pain incorrect responses, albeit this was irrespective of Manipulation (i.e., pre/post cold-pressor/warm water task). Hence, given it was expected that participants in the pain condition would recognise more pain/pain-illness related solutions they generated in the second Interpretation Bias Task (post pain-induction) when asked to identify these one month later (using a yes/no paradigm), hypothesis 4 was rejected. However, it should be noted that an interation was observed for the recognition bias data pre cold-pressor task. To recap, both groups obtained a significantly higher percentage of non-pain correct than non-pain incorrect responses, however, the magnitude of the effect was pronounced for those in the no pain condition.

In considering first the null effects, it should be noted that recognition biases have not typically been measured in pain research, and to date, no studies exploring combined cognitive biases (including AB, IB and Recall) have also included recognition. Recognition paradigms, including the ability to utilise Signal Detection, enable richer evaluation of participant responses (both with respect to correct and incorrect responses) than free recall methodology. One study that might be relevant, however, is that by Forkmann et al. (2016; Chapter 1 section) in which participants were presented with an encoding task concurrently with or without themal heat pain. Next, participants were presented with a surprise recognition task. Findings showed that the experience of pain during the encoding task impaired recognition performance. More specifically, participants displayed a lower recognition for images that were presented concurrently with heat stimulation. This is partially consistent with the interaction effect observed. To expand, whilst we found no differences in pain experience (i.e. cold-pressor or warm water) in recognition of the pain-words, we did find an advantage for the recognition of non-pain words for participants in the non-pain group. That is, participants in the non-pain condition were more likely to correctly identify ‘old’ non-pain words and correctly reject ‘new’ non-pain words, then participants in the pain group. This suggests that being subject to pain did impair recognition memory. However, more research is needed, given the paradigm used in the present thesis and that of Forkmann et al.,

(2016) differed quite considerably and that the investigation of recognition biases have still received little empirical attention to date. This is despite a recent review of the chronic pain and memory literature providing evidence of impairments in working and long-term memory, with chronic pain sufferers displaying more difficulties in encoding and retrieval processes than controls (Mazza et al., 2017), which again is consistent with the interaction effect observed.

As with recall bias, correlational analyses revealed a negative relationship between pain threshold and the number of pain/pain-illness words correctly recognised 1-month post cold-pressor task for participants in the Pain condition. That is the greater a participants pain sensitivity, the greater their recognition accuracy of pain/pain-illness related words one-month later. Whilst this finding again supports the general role of pain sensitivity in cogntive biases, it also suggests that this individual difference may influence multiple forms of memory bias, adding credence to the notion that future research should measure both recall and recognition biases.

5.4.1.4 Limitations and Future Research

Firstly, it should be noted that the study was underpowered. Prospective G*Power analysis highlighted 82 participants (study 3, $n = 48$) would be needed to achieve a medium effect size and power of .80. However, the sample size in the present study reflected the amount of time available for data collection due to the impact of the COVID-19 pandemic.

Secondly, previous research has argued that future studies should counterbalance the order of paradigms used to measure cognitive biases given it would enable greater examination of their interplay (Schoth et al., 2018). However, due to the nature of the AB task, presenting images of a high/medium pain intensity and high/medium threat value may have primed participants in the IB task towards pain-related interpretations. Therefore, to eliminate this risk the IB tasks were always presented first and thus is a strength of the present study. That said, it should be noted that all other elements of the study were counterbalanced.

Thirdly, a further point of consideration is the duration between the recall and recognition task (1-month). Whilst more longditudinal research is needed, measuring cognitive biases over multiple durations (e.g., 1 week, 1 month) would help to provide further insight as to whether one

form of bias influences others. Indeed, Rusu et al. (2018) highlights that it remains unknown as to whether cognitive biases are vulnerability factors that contribute to the development and maintenance of chronic pain, or whether they result as a consequence of long-term exposure to pain. Hence, further research employing prospective designs are needed in both acute and chronic pain populations to further understand the interplay of cognitive biases in the development and maintenance of chronic pain.

Lastly, the findings of the present study have revealed that individuals have differing pain thresholds and tolerances – thus for some individuals allocated to the Pain conditon, a single cold-pressor experience may not have been 'potent enough' to mediate/moderate cognitive biases, as potentially their sensitivity to pain and pain tolerances are higher. Future research should therefore include a measure of pain sensitivity to examine how this influences how individuals interpret, attend to and remember pain-related information following a pain experience. Such findings may also have implications for existing pain theories. To expand, the Integrated Functional Contextual Framework (Van Ryckeghem et al., 2019) has been particularly influential in it's propositions that cognitive biases are functional, dynamic and inter-related. Indeed, a key claim of this framework is that it is the inflexibility or ridgitity in the way people attend, interpret, and remember pain information that results in negative pain outcomes. In this context, it may be that pain sensitivity is a vulnerability factor that contributes to this inflexibility/ridgidity through its effects on executive functioning. For example, individuals with higher levels of pain sensitivity may have poorer executive functioning (e.g., reduced attentional control, deficient inhibition function), which then when an individual experiences pain, increases the potency of pain-related cognitive biases (i.e., hypervigilance, threat value). This then may subsequently influence the trajectory from acute to chronic pain, and/or maintain distress and suffering. Accordingly, a recent systematic review of the pain and executive functioning literature found that in chronic pain patients, stronger pain was associated with worse executive functioning (Bunk et al., 2019). Hence, actively integrating vulnerablity factors, and how they may interact with motivational and contextual factors, would be particularly fruitful in future research to unpick the complex relationship between cognitive biases and pain.

5.4.1.5 Conclusion

The aim of the present study was to examine attention, interpretation and memory (including recall and recognition) biases in a pain versus no pain situation. Overall, there was limited evidence to suggest that a pain (verus no pain) situation is sufficient to induce cognitive biases towards pain/pain-illness related information. That said, all participants displayed AB during the early and later stages of attention for high and low pain images, regardless of pain manipulation condition. This finding supports the notion that ABs to pain-related information are ubiquitous (Blaisdale-Jones et al., 2021) and relevant to all (Maratos and Pessoa, 2019). An interesting result of the present study was that subjecting participants to a pleasant experience increased latency to first fixation towards Low Pain images and recall of words used in the pain scenarios . The implications of these findings need to be explored further, but it could be that providing individuals with a pleasant experience prior to pain, may increase subsquent pain coping (or at least negate avoidance of such). The results also support that an acute pain experience can enhance immediate memory (i.e., recall) for both pain and non-pain items, supporting the notion that pain may strengthen high-priority memory traces. With respect to delayed memory (i.e, recognition) the results suggest that a painful experience can negatively affect retrieval of information at a later date. Finally, correlations between cognitive biases and pain measures indicated that pain threshold negatively correlated with interpretation, recall and recognition bias, while pain tolerance correlated negatively with interpretation and first fixation proportion for high pain images. Considering the above, it may be that pain sensitivity is an important factor in predicting cognitive biases and pain coping and thus requires investigation. However, to fully understand the extent to which cognitive biases influence the processing of pain-related information further research in a chronic pain sample is also warranted. Consequently, a study measuring cognitive biases in a chronic pain sample is presented in Chapter 6.

Chapter 6 **Exploring Interpretation and Memory Biases in Chronic Pain and Non-Pain Control Participants.**

6.1 Introduction

Theoretical models of pain, including the Integrated Functional Contextual Framework (IFCF, Van Ryckeghem et al., 2020), posit that cognitive biases do not operate in isolation, but instead interact with one another in a cyclical fashion to impact pain chronicity. These biases include the interpretation of ambiguous information in a pain/pain-illness related manner (Interpretation Bias, IB), and the ability to selectively recall pain and/or illness associated information from memory (Memory Bias, MB). Yet, only six studies have investigated more than one cognitive bias within the context of a single study with chronic pain patients (Todd et al., 2016; Hughes et al., 2017; Schoth et al., 2018, 2019; Chan et al., 2020; Blaisdale-Jones et al., 2021). Thus, the influence, direction, and nature of these biases remains poorly understood, highlighting an urgent need for more cross-bias research. However, due to COVID-19 2020-2021 restrictions, measurement of Attentional Biases (AB) was beyond the scope of this study given the vulnerable nature of this participant group preventing in-person data collection. Hence, despite previous research demonstrating mixed findings for the role of AB in chronic pain or otherwise (Schoth et al., 2018; Schoth et al., 2019), the focus of this Chapter/research was on examining IB and MB (Recall and Recognition) in a chronic pain (CP) and non-pain control (NPC) sample.

In respect to IB, early evidence demonstrated that adults suffering from chronic pain display IB, characterised by a tendency to interpret ambiguous information in a pain/pain-illness related fashion (Pincus et al., 1994; Pincus et al., 1996; McKellar et al., 2003). However, scrutiny of the initial paradigms (Homophonic/Homographic Response Tasks) used to measure IB (including lack of appropriate stimuli, response biases, see Schoth et al., 2020) led to the development of more sophisticated measures of IB, including the Adolescent Interpretation Bias Task (AIBT, Heathcote et al., 2016). Using the AIBT, negative IBs have been found in youth with

chronic pain (Heathcote et al., 2017, Lau et al., 2019), adults with chronic pain (Chan et al., 2020), and more recently healthy adults reporting more recent pain experiences (see Chapter 4, Gaffiero et al., 2022). However, like traditional IB paradigms, the AIBT has received criticism. Notably, for the use of a forced-choice response format which constrains participants to pre-determined interpretations which may not reflect their own personal interpretation of a scenario; and a lack of control stimuli, which may inadvertently prime (pain) responding and/or contribute to demand characteristics.

Gaffiero et al. (2022) used a free and forced version of the original AIBT to develop and validate two ambiguous scenario stimulus sets suitable for measuring IB in adults with pain, consisting of: one free-response and one forced-response stimulus scenario sets. A key strength of these scenario sets is that they enable researchers to select a scenario set(s) in accordance with their own design needs. For example, the free-response ambiguous scenario set can be used within a free-response AIBT to allow participants to provide their own personal interpretation of each scenario. In addition to the free-response and forced-response stimulus sets, a control scenario set was also generated to be used alongside either stimulus set to minimise issues surrounding priming, order effects and demand characteristics. This allows ecological validity of the paradigm to be increased, enabling researchers to more comprehensively investigate whether adults with chronic pain display IB for pain/pain-illness information with fewer stimulus/paradigm confounds.

With respect to MB, there is evidence to support the notion that adults with chronic pain exhibit enhanced recall for pain-related information (Pincus & Morley, 2001). Such findings are consistent with Bower's (1981) Associative Network Theory. This asserts that repeated activation of a 'pain node' activates corresponding nodes containing memories for pain-related experiences. Hence, the persistent nature of chronic pain is thought to contribute to the development of MB via a reduction in the threshold for which pain-congruent material is processed. This increases the frequency of pain nodes becoming activated, resulting in pain-related memories more regularly entering consciousness. This theory also has some similarities to motivational relevance (Maratos & Pessoa, 2019). In this theory, relevance (not threat) is suggested as the most important factor influencing biases. In pain patients, pain is relevant. Thus, in this context attentional prioritisation

of pain-related information generates a potentially protective response (if necessary), with brain networks then influencing cognitive biases to painful stimuli. Translated to memory, the details of situations that require a protective response are therefore encoded into long-term memory and become re-activated with repeated exposure. However, there is also contradictory evidence reporting no evidence of a recall bias in pain patients (e.g., Karimi et al., 2016; Schoth et al., 2019). Schoth et al., (2020) conducted a systematic-review and meta-analysis of the pain and recall bias literature and concluded that the evidence is currently 'inconclusive'. Hence, further research is needed to assess whether chronic pain patients display biased recall for pain-related information.

Whilst much of the pain literature has focused on recall as the primary outcome measure of MB, there is some evidence to suggest that depressed adults with CP display biased recognition, exhibited via increased recognition of pain-related words (Pincus et al., 1995; Schwarze et al., 2012). In recall tasks, participants are presented with previously learned information and are asked to retrieve it without the aid of external cues, whereas in recognition tasks participants are presented with previously learned information and make judgements as to whether (or not) items are new (have not been seen before) or are old (have been seen before). This is important because recognition paradigms can be argued to be more ecologically valid than free-recall paradigms, given the presentation of cues (e.g., words), allowing for comparison processes between the available and stored information to be investigated (Haist et al., 1992). That said, like the recall bias literature, findings for recognition biases in adults with chronic pain are also mixed. Studies have reported impaired recognition memory for images presented concurrently with painful heat stimulation in **healthy** participants (Forkmann et al., 2016), impaired recognition performance in **chronic pain** patients relative to healthy controls in a Remember/Know paradigm (Grisart et al., 2007), and no **differences** in the number of pain adjectives correctly recognised amongst chronic pain patients and healthy controls (Flor et al., 1997). Gaffiero et al. (in prep, Chapter 6) allocated a group of healthy participants to a pain (cold-pressor task) or no pain (warm water task) condition and measured ***both*** recall and recognition biases for pain/pain-illness and/or non-pain/non-pain illness solutions generated in an ambiguous scenario IB task. With respect to recall and recognition a single experience of pain was not sufficient to bias recall and recognition memory towards pain-related information (although it was found that a single experience of the control, arguably

pleasurable experience, did). Hence, the exact nature of both recall and recognition biases, in respect to pain experiences, is unclear. For example, do adults with chronic pain display biased recall and/or recognition for pain-related information? …and if so, does this change over time?

To date, only two studies have measured IB and MB (including AB) within the context of a single study (Schoth et al., 2018; 2019). Schoth et al., (2018) first conducted a preliminary investigation pertaining to cognitive biases in pain by recruiting two group of participants: those with Chronic Headache (CH, n = 17) and Healthy controls (HC, n = 20). To measure AB, IB and MB participants completed a spatial cueing task, sentence generation task and free recall task respectively. There was no evidence of an AB, however IB and MB were observed for sensory-pain words in the CH group. To expand, the CH group provided significantly more pain responses to sensory-pain words in the IB task and recalled significantly more sensory-pain words in the free recall task compared to their HC counterparts. Hence, the authors concluded that the study findings provide evidence of IB and MB in individuals with CH. Schoth et al., (2019) later recruited another sample of participants with CH (n = 28) and HC (n = 34), measuring AB, IB and MB via a visual-probe task, sentence generation task and free recall task respectively. Unlike their preliminary study, no differences in MB were observed between the two groups. However, AB and IB differences were observed – such that participants in the CH group showed an AB for pain-related words presented during initial orienting (i.e., 500ms), and generated more pain responses to sensory-pain words in the sentence generation task. Regarding key conclusions, whilst Schoth et al. (2019) found evidence of AB and IB in a CH sample, they noted the discrepancy in findings relating to AB and MB between the two investigations. Hence, further research is required to gain a more detailed insight as to the nature of MB (and AB) in pain, and whether this exerts itself in the form of recall, recognition biases, or both.

Considering the above, the aim of the present study was to investigate interpretation and memory (recall and recognition) biases in a sample of chronic pain patients as compared to non-pain controls. As stated above, investigation of AB was not possible due to COVID-19 restrictions. It was hypothesised that:

i) Participants with chronic pain would interpret more ambiguous scenarios in a pain/pain-illness related manner compared to their non-pain counterparts.

ii) Participants with chronic pain would recall more pain/pain-illness related solutions generated in the ambiguous scenarios task compared to their non-pain counterparts.

iii) Participants with chronic pain would correctly recognise more pain/pain-illness related solutions generated in the ambiguous scenarios task compared to their non-pain counterparts.

iv) Relationships would emerge between Interpretation and Memory (recall/recognition) biases, such that as the number of scenarios interpreted in a pain-related manner increased in the chronic pain group, so to would the number of pain words correctly recalled and recognised.

To investigate the above hypotheses, the modified AIBT paradigm developed by Gaffiero et al (2022; Chapter 4) was used to measure interpretation, recall and recognition biases. Participants were first presented with a demographic questionnaire prior to completing the DASS-21 scale. Next, participants completed a free-response ambiguous scenarios task to measure IB, followed by completion of the RPEQ. Participants were then presented with a surprise free-recall task and were asked to write down as many of the AIBT solutions they could remember that they had provided to complete the scenarios in the ambiguous scenarios task earlier. One-month later, participants completed a personalised 'Yes-No' recognition task which presented their personal solutions to each ambiguous scenario (i.e., Old Stimuli) intertwined with filler (i.e., New Stimuli) solutions to assess recognition bias. Due to COVID-19 restrictions the entire study was conducted on-line.

6.2 Method

6.2.1 Participants

Participants were recruited via distribution of an online study advertisement. This advert stated inclusion criteria of fluency in English, normal or corrected-to-normal vision and of age 18 or over. To obtain participants from pain populations stratified sampling was used. That is, to attract participants who suffered from a pain-related condition/syndrome, specific forums of social media sites such as Reddit (i.e., r/Chronic Pain), Facebook (Pain Concern, Northamptonshire Chronic Pain Support) and Health Unlocked (Chronic Pain Forum, Osteoarthritis Action Alliance) were approached. To attract 'non-pain' participants, the University of Derby's Psychology Research Participation Scheme was used. This resulted in recruitment of an International (UK and wider) opportunity sample of 153 participants, with participants recruited from Facebook (5.2%), Health Unlocked (13.1%), the University of Derby's Psychology Research Participation Scheme (8.5%) Reddit (53.6%), Social-media (2.6%), Website/Forums (1.4%) or a General Advertisement (15.7%). Prospective power analysis using G*Power indicated that to achieve a medium effect size (.25) and acceptable power (i.e., 0.8; with alpha set at 0.05, one-tailed) for a repeated measures design, the calculated sample size required was 82. This power analysis was conducted based on one between-subjected variable (group: chronic pain, non-pain control) and two within-subjects' factors (manipulation: pre, post; stimulus type: ambiguous, filler).

The top 3 participant nationalities were American (37.91%), British (35.95%) and Canadian (5.88%). Most participants reported being White in ethnicity (90.19%) and English was the most reported first language (85.62%). With respect to highest educational level, participants reported GCSE (14.38%), A-level (15.69%), Undergraduate Degree (30.17%) or Postgraduate Degree (16.34%).

All 153 participants undertook the first part of this study (Mean Age = 33.61, SD = 14.74; Female = 108, Male = 37, Other = 6, Prefer not to say = 2). Of these, 76 participants were assigned to the non-pain control group and 77 to the chronic pain group. To expand, 77 reported

experiencing pain for over 12 weeks (i.e., 3 months), with 68 reporting a diagnosed pain condition (not diagnosed/specified = 9). The three most reported chronic pain conditions included Arthritis (including Osteoarthritis, Rheumatoid Arthritis, Psoriatic Arthritis, Pseudogout and Seronegative Arthritis, 20.8%, *n* = 16), Fibromyalgia (19.50%, *n* = 15) and Chronic Headache (including Migraine and Occipital Neuralgia, 10.4%, *n* = 8). On average, these 77 participants reported experiencing pain for 11.23 years (SD = 8.05 years). The 76 participants assigned to the healthy control group did not report experiencing pain over the last 3 months or suffering from a pain-related condition. Thus, the initial chronic pain group consisted of 77 participants (Mean Age = 39.09, SD = 16.75; Female = 65, Male = 7, Other = 4, Prefer not to say = 1) and the Non-pain control group consisted of 76 participants (Mean Age = 28.07, SD = 9.69; Female = 43, Male = 30, Other = 2, Prefer not to say = 1). Mental Health Diagnoses were reported in both the chronic pain (Anxiety = 6.5%, Depression = 22.1%, Both = 50.6%, None = 20.8%) and non-pain control group (Anxiety = 7.9%, Depression = 13.2%, Both = 21.1%, None = 57.8%).

At one-month follow-up, 42 dropouts were observed (chronic pain group, *n* = 20, non-pain control group, *n* = 22). Thus, the retention rate was high (72.55%) and the final one-month follow-up sample comprised a total of 111 participants, 57 participants in the chronic pain group, (Mean Age = 40.37, SD = 16.47; Female = 49, Male = 5, Other = 2, Prefer not to say = 1), and 54 participants in the Non-pain control group (Mean Age = 28.29, SD = 9.96; Female = 34, Male = 18, Prefer not to say = 2).

For compensation of their time and commitment to the study, University of Derby students (8.5%) received course credit. Participants from the wider population were entered into a prize draw, of which there was a 1 in 15 chance of winning a £15 E-Voucher. The study was approved by the College of Health, Psychology and Social Care Ethics Committee at the University of Derby and informed consent was gained from each participant.

6.2.2 Design

The study employed a mixed-measures design with three independent variables. One between-subjects variable: pain group (chronic pain, pain-free – obtained post-hoc) and two within-subject's variables. These were, specific to the interpretation bias task (**1**) scenario type (ambiguous, filler), and specific to the memory bias tasks (**2**) word type (pain/pain-illness related, non-pain/non-pain illness related). The dependent variables included the number of pain/pain-illness and non-pain/non-pain illness interpretations (interpretation bias task), the number of pain/pain-illness related solutions and non-pain/non-pain illness solutions correctly recalled (surprise free recall task), and the number of hits, misses, false alarms and correct rejections using Signal Detection Methodology for the pain/pain-illness solutions and non-pain/non-pain illness solutions (post 1-month recognition task).

6.2.3 Materials

The entirety of the experiment was presented using Qualtrics (UT, Provo) software, given the COVID-19 2020-2021 restrictions and the vulnerable nature of the chronic pain group preventing in-person data collection. For brevity, where questionnaires and tasks were the same as in Chapter 5 repeat information is not provided.

6.2.3.1 Demographic Questionnaire

Participants were asked to complete a short demographic questionnaire comprising their age, gender, nationality, educational level, first language, history of Anxiety and/or Depression, whether they had experienced pain for more than 12 weeks, and if they had a diagnosed pain-related condition/syndrome. Participants who answered "yes" to experiencing pain for more than 12 weeks were also asked to estimate how long they had been struggling with pain (in months and years) as close to as they could recall.

6.2.3.2 DASS-21

Depression, Anxiety and Stress was measured using the DASS-21 (see Chapter 5, section 5.2.3.2).

6.2.3.3 Recent Pain Experiences Questionnaire

Recent Pain Experiences was measured using the RPEQ (see Chapter 5, section 5.2.3.3).

6.2.3.4 Experimental Paradigms

6.2.3.4.1 *Ambiguous Scenarios Task (Interpretation Bias)*

Interpretation bias was measured using a free response version of the AIBT (as described in Chapter 5, section 5.2.3.5.1). Slight modifications were made for running this task online (versus in person). Instead of scenarios being split into two separate interpretation bias tasks (as was the case in Chapter 5), participants were randomly presented with individual scenarios in a single interpretation bias task. Therefore, 37 scenarios were presented in total. These comprised: 1 practice trial, 18 ambiguous scenarios and 18 filler scenarios. All other elements of this task remained the same as described in Chapter 5.

6.2.3.4.2 *Memory Bias Tasks*

To examine whether the experience of pain influences the development of memory biases and whether this changes over time two memory bias tasks were employed. The first was a recall bias task. No differences were made to the task as described in Chapter 5 (section 5.2.3.5.3). The second was a recognition bias task. No differences were made to the task as described in Chapter 5 (section 5.2.3.5.4). For clarity, duplicate responses accounted for 84 out of 1656 responses and therefore 4.89% of the data.

6.2.4 Procedure

Upon procurement of informed consent, participants were asked to complete the short demographic questionnaire before completing the DASS-21 scale. Next, participants completed

the Ambiguous Scenarios Task. To avoid any issues associated with the recency effect, the RPEQ was completed prior to the Surprise Free Recall Task. Upon completion of the Surprise Free Recall Task participants were debriefed, reminded that they would be contacted 1-month later to take part in the second phase of the study, and thanked for their time. This phase of the study took approximately 30 minutes.

One month (28 days) post-experiment, participants were sent an email that contained a Qualtrics link to their personalised task. For each personalised task, informed consent was gained, after which participants completed the Delayed Recognition Task before being presented with a debrief sheet and thanked for their time. For each participant, in accounting for duplication, the number of words presented varied from 72 (no duplication) to 62 (6.94% duplication in the free recall task). On average, participants took 15 minutes to complete this phase of the research. Thus, in total the entire study took 45 minutes to complete.

6.2.5 Data Screening

Data screening was pursued to investigate any differences in populations (chronic pain, non-pain controls). To assess whether there were differences in ***gender*** between the chronic pain (CP) and Non-pain control (NPC) groups, participants who preferred not to declare their gender (n = 2) and/or cited their gender as "other" (n = 6) were excluded from the analysis. Significant differences in the number of males and females were observed between the CP and NPC groups, χ^2 (1) = 18.773, p = <.001. To expand, there were more males in the NPC (n = 30, 81.1%) compared to the CP group (n = 7, 18.9%), and more females in the CP (n = 65, 60.2%) compared to NPC (n = 43, 39.8%) group. Significant differences in ***age*** were also observed between the CP and NPC groups, with the CP group older (M = 39.09, SD = 16.75) than the NPC group (M = 28.06, SD = 9.69); t (122.043) = -4.992, p = <.001, *two-tailed*). The magnitude of the differences in the means (mean difference = -11.02, 95% *CI*: -15.39 to -6.65) was large (eta squared =.17, Cohen 1988, pp.284-7).

As outlined in **Table 6.1**, on average participants in the CP group reported moderate levels of Depression and Stress and mild levels of Anxiety. Whereas NPC reported normal levels of Anxiety and mild levels of Depression and Stress. Independent Samples T Tests revealed these differences to be significant, with the CP group reporting significantly higher levels of ***Depression*** t (151) = -3.193, p = .001, ***Anxiety*** t (151) = -4.173, p = < .001, and ***Stress*** t (151) = -3.112, p = .002 compared to their NPC counterparts. As expected, differences were further observed for the ***RPEQ*** data, with the CP group reporting significantly higher pain frequency t (151) = -19.038, p = <.001, pain interference t (140.389) = -13.727, p = <.001, average pain intensity t (145.083) = -13.058, p = <.001 and worst pain intensity t (130.441) = -14.755, p = <.001.

Table 6.1: Means and SDs for the DASS-42 and Recent Pain Experiences Questionnaire by Participant Group (Chronic Pain, Non-pain controls).

Questionnaire Indices	*Overall* Mean (SD)	*Chronic Pain* Mean (SD)	*Non-pain controls* Mean (SD)
Depression (DASS-42)	15.33 (12.27)	18.39 (12.26)	12.23 (11.56)
Anxiety (DASS-42)	10.57 (8.90)	13.40 (9.37)	7.70 (7.41)
Stress (DASS-42)	15.47 (10.16)	17.95 (10.32)	12.97 (9.42)
Pain Frequency (last 3 months)	3.64 (2.14)	5.43 (1.20)	1.84 (1.12)
Pain Interference (last 3 months)	3.63 (3.24)	6.01 (2.46)	1.21 (1.83)
Average Pain Intensity	5.67 (3.28)	8.16 (1.65)	3.14 (2.47)
Worst Pain Intensity	3.43 (2.70)	5.38 (2.05)	1.46 (1.64)

A series of factorial mixed ANOVAs were conducted to examine whether there were any differences in DASS-42 scores between groups (NPC, CP) at initial assessment and at 1-month follow-up. The ANOVAs for Anxiety and Stress revealed no significant differences between gender or time point, nor was there an interaction ($p > .05$). However, for depression, a significant main effect of group was observed $F(1,104) = 8.203$, $p = .005$, $\eta^2 p = .070$, such that depression scores were higher for the CP group. Additionally, a significant main effect of time point was observed $F(1,104) = 4.854$, $p = .030$, $\eta^2 p = .043$, such that depression scores were lower at the 1-month follow up. A group by timepoint interaction effect was further observed $F(1,104) = 4.297$, $p = .041$, $\eta^2 p = .038$ (**see Figure 6.1),** this demonstrates that depression scores for the pain group decreased over the one-month time period. To expand, Bonferroni-correction (alpha = .0125) post-hoc comparisons revealed a significant difference in depression scores between groups at baseline ($p = .001$, $d = .52$), where individuals with chronic pain scored significantly higher on depression compared to non-pain controls. There was no significant difference in depression between groups at the 1-month follow up, albeit this was approaching significance ($p = .02$, $d = .38$). Moreover, no significant difference was observed across timepoints for the non-pain control group ($p = .46$). However, a significant difference was observed across timepoints for the CP group ($p = .004$, $d = .37$), where the CP group exhibited lower levels of depression at one-month. The means and SDs are displayed in **Table 6.2**.

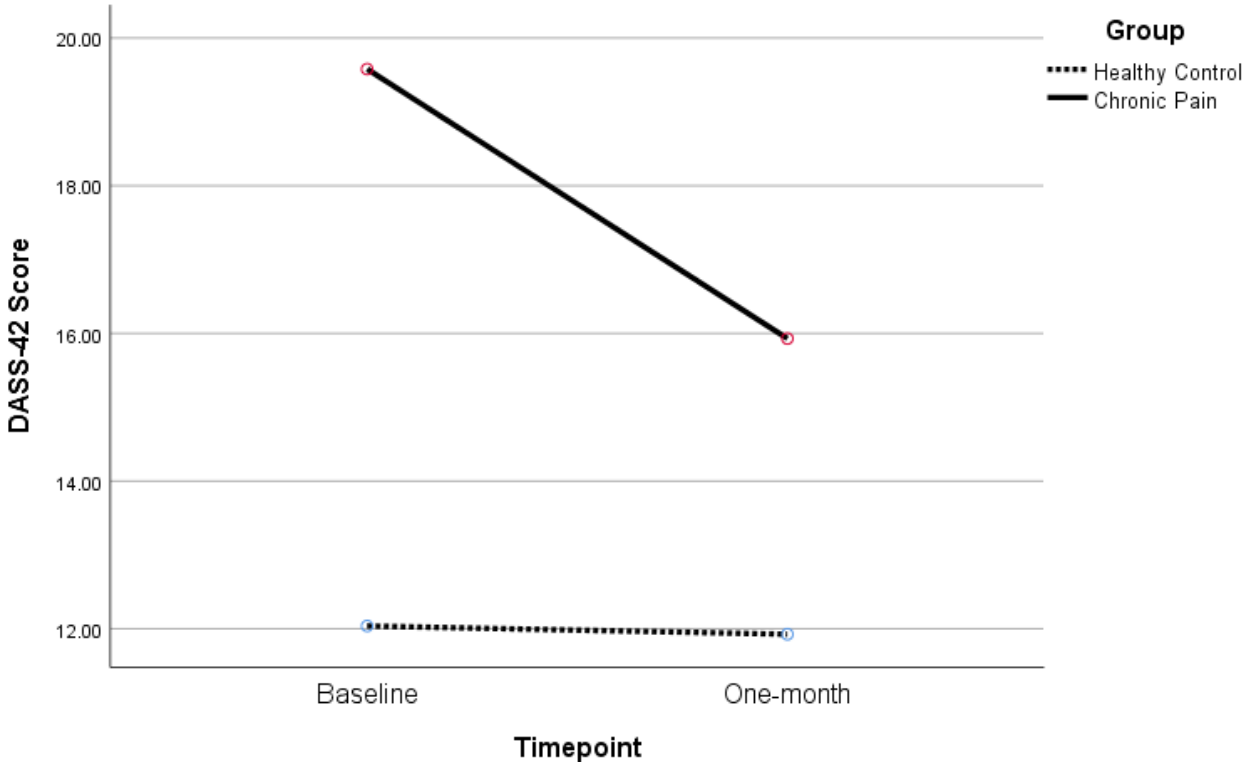


Figure 6.1: DASS-42 Scores by Group and Timepoint.

Table 6.2: Mean Depression Scores (SD) Across Groups (CP/NPC) at Initial Assessment and 1-Month Follow-Up.

	Initial Assessment	1-Month Follow-Up	Total
Non-pain controls	12.037 (11.940)	11.926 (10.836)	12.107 (11.223)
Chronic Pain	19.579 (13.119)	15.930 (9.950)	17.343 (11.358)
Total	15.910 (13.063)	13.982 (10.537)	

A series of factorial mixed ANOVAs were also conducted to examine whether there were any differences in RPEQ scores between groups (NPC/CP) at initial assessment and at 1-month follow-up. The ANOVAs for Pain Interference and Pain Frequency revealed no significant differences between gender or time point, nor was there an interaction ($p > .05$). In contrast, but as expected, a significant main effect of group was observed for average pain intensity $F(1,104) = 114.315$, $p < .001$, η^2 p = .512, such that average pain intensity was higher for the CP group. There was no main effect of time point $F(1,104) = .614$, p = .435, η^2 p = .006, however, a significant interaction effect between group and time point was observed $F(1,104) = 5.571$, $p = .020$, η^2 p = .049 (**see Figure 6.2**). This appeared to simply reflect a slight increase in pain intensity for the control group. To expand, Bonferroni-correction (alpha = .0125) post-hoc comparisons revealed a significant difference in average pain intensity scores between groups at initial assessment ($p < .001$, $d = 2.11$), where individuals in the CP group scored significantly higher on average pain intensity compared to non-pain controls. There was also a significant difference at the 1-month follow up ($p < .001$, $d = 1.87$), such that individuals in the CP group again scored higher on average pain intensity compared to the NPC group. Despite not reaching statistical significance, the interaction effect appears to be driven by an increase in average pain intensity between initial assessment and 1-month follow up for the NPC ($p = .015$, $d = .30$) group. No difference was observed in average pain intensity from baseline to 1-month for the CP group ($p = .134$). The means and SDs are displayed in **Table 6.3**.

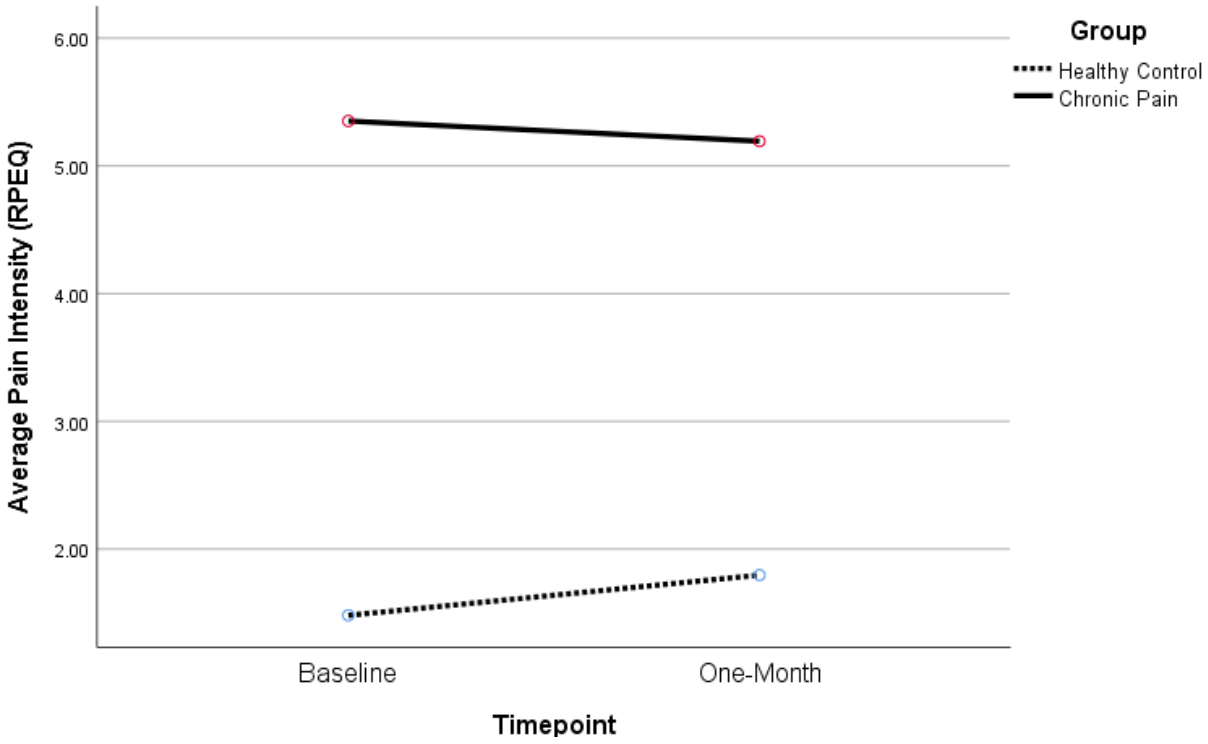


Figure 6.2: Average Pain Intensity by Group Status and Timepoint.

Table 6.3: Mean Average Pain Intensity Scores (SD) Across Groups (CP/NPC) at Initial Assessment and 1-Month Follow-Up.

	Initial Assessment	1-Month Follow-Up	Total
Non-pain controls	1.482 (1.657)	1.796 (1.419)	1.60 (1.55)
Chronic Pain	5.351 (2.117)	5.193 (2.133)	5.298 (2.07)
Total	3.469 (2.716)	3.541 (2.489)	

As expected, a significant main effect of group was also observed for worst pain intensity $F(1,104) = 129.472$, $p < .001$, η^2 p = .543, where worst pain intensity was higher for the CP group, but there was no main effect of timepoint $F(1,104) = .245$, $p = .622$, η^2 p = .002. However, a significant interaction effect between group and time point was observed $F(1,104) = 4.804$, $p = .031$, η^2 p = .042 (**see Figure 6.3)**. Bonferroni-correction (alpha = .0125) post-hoc comparisons revealed a significant difference in worst pain intensity scores between groups at initial assessment ($p < .001$, $d = 2.39$), where individuals in the CP group scored significantly higher on worst pain intensity compared to non-pain controls. There was also a significant difference at the 1-month follow up ($p < .001$, $d = 1.76$), such that individuals in the CP group again scored higher on worst pain intensity. Despite no significant difference being observed between initial assessment and 1-month follow up for the NPC ($p = .056$) or CP ($p = .073$) groups, the interaction effect appears to be driven by the NPC group reporting increased worst pain intensity at one-month, and the CP group reporting reduced worst pain intensity at 1-month. The means and SDs are displayed in **Table 6.4** below.

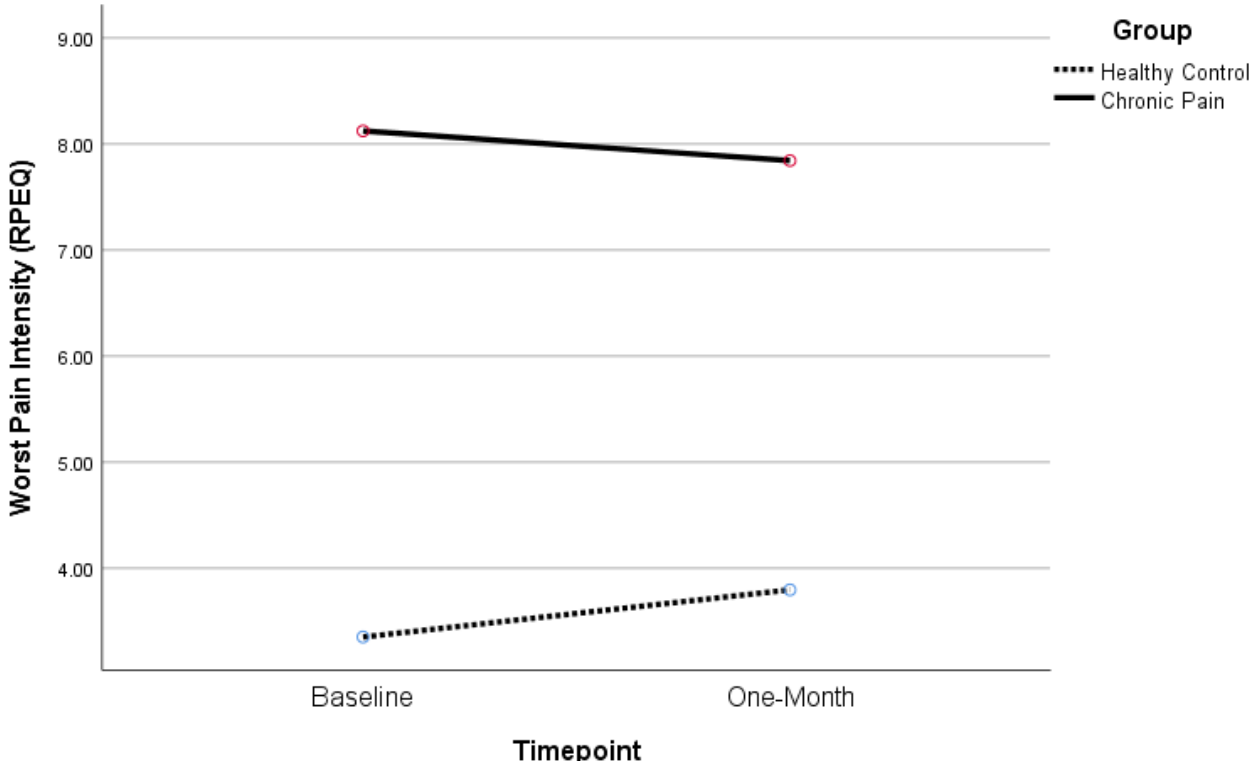


Figure 6.3: Worst Pain Intensity by Group Status and Timepoint

Table 6.4: Mean Worst Pain Intensity Scores (SD) Across Groups (CP/NPC) at Initial Assessment and 1-Month Follow-Up.

	Initial Assessment	1-Month Follow-Up	Total
Non-pain controls	3.352 (2.578)	3.796 (2.673)	3.41 (2.56)
Chronic Pain	8.123 (1.691)	7.842 (1.801)	8.029 (1.71)
Total	5.802 (3.224)	5.874 (3.037)	

6.3 Results

6.3.1 Exploring Interpretation Bias between Chronic Pain and Non-pain control Participants

To investigate hypothesis 1, that participants in the CP group would interpret more ambiguous scenarios in a pain/pain-illness related manner compared to their non-pain counterparts, an Independent T-Test was conducted on the IB index scores (**see Table 6.5**). There was no significant difference in IB Index between the NPC and CP Groups $t(151) = -.766$, $p = .223$.

Table 6.5: Mean IB Index (SD) for Group in the Ambiguous Scenarios Task.

	IB Index
Chronic Pain	-.52 (6.46)
Non-pain controls	-1.30 (6.18)
Total	-.91 (6.31)

6.3.2 Exploring Memory (Recall Bias) between Chronic Pain and Non-pain control Participants

To investigate Hypothesis 2, that participants in the chronic pain group would recall more pain/pain-illness related solutions generated in the ambiguous scenarios task compared to their non-pain counterparts, a 2 (Group: CP, NPC; between-subjects variable) x 2 (Free Recall Category: pain/pain-illness, non-pain/non-pain illness; within-subjects variable) Mixed-Measures ANOVA was conducted. There was no significant main effect of Free Recall Category $F(1, 151) = .316$, $p = .575$, $\eta^2 p = .002$. There was no significant main effect of group $F(1, 151) = .609$, $p = .436$, $\eta^2 p = .004$. Lastly, there was no significant interaction effect between Free Recall Category and Group $F(1, 151) = .939$, $p = .334$, $\eta^2 p = .006$ (See **Table 6.6** below for Mean/SD).

Table 6.6: Mean Frequency Scores (SD) for Free Recall Category and Group in the Free Recall Task

	Free Recall Category Pain/Pain-illness	Free Recall Category Non-Pain/Non-Pain illness	Total
Chronic Pain	2.89 (1.83)	2.98 (2.19)	2.94 (2.01)
Non-pain controls	3.30 (2.05)	2.96 (2.07)	3.13 (2.06)
Total	3.09 (1.95)	2.97 (2.12)	

6.3.3 Exploring Recognition Biases between Chronic Pain and Non-pain control Participants

To investigate Hypothesis 3, that participants in the chronic pain group would correctly recognise more pain/pain-illness related solutions generated in the ambiguous scenarios task compared to their non-pain counterparts, a 2 (Group, CP, NPC, between-subjects variable) x 2 (Response type; Pain correct, Pain incorrect, within-subjects variable) Factorial Mixed-Measures ANOVA was conducted. Levene's test violated assumptions of homogeneity of variance, therefore the Greenhouse-Geiser correction was observed. The analysis revealed a significant main effect of response type $F(1, 104) = 99.156$, $p < .001$, $\eta^2 p = .488$, such that there were significantly higher pain correct responses than pain incorrect responses. There was no significant main effect of group $F(1, 104) = <.000$, $p = 1.00$, $\eta^2 p = <.001$. However, importantly, a significant group x response type interaction effect was observed $F(1, 104) = 4.808$, $p = .031$, $\eta^2 p = .044$ (**see Figure 6.4**).

Bonferroni-correction (alpha = .0125) post-hoc comparisons were conducted to investigate the significant interaction effect further. This revealed no significant differences between groups in the percentage of pain correct responses ($p = .016$, $d = .43$), nor the percentage of pain incorrect responses ($p = .016$, $d = .39$). Significant differences were observed, however, between the percentage of pain correct and incorrect responses, such that higher pain correct responses were observed for the NPC ($p < .001$, $d = 1.46$) and CP ($p < .001$, $d = .65$) group (see **Table 6.7** for Mean/SD). The interaction effect therefore must reflect the greater difference (represented by the

steeper line) for the NPC group (as illustrated in Figure 6.4), indicating a higher percentage of pain correct and a lower percentage of pain incorrect responses, than their CP counterparts.

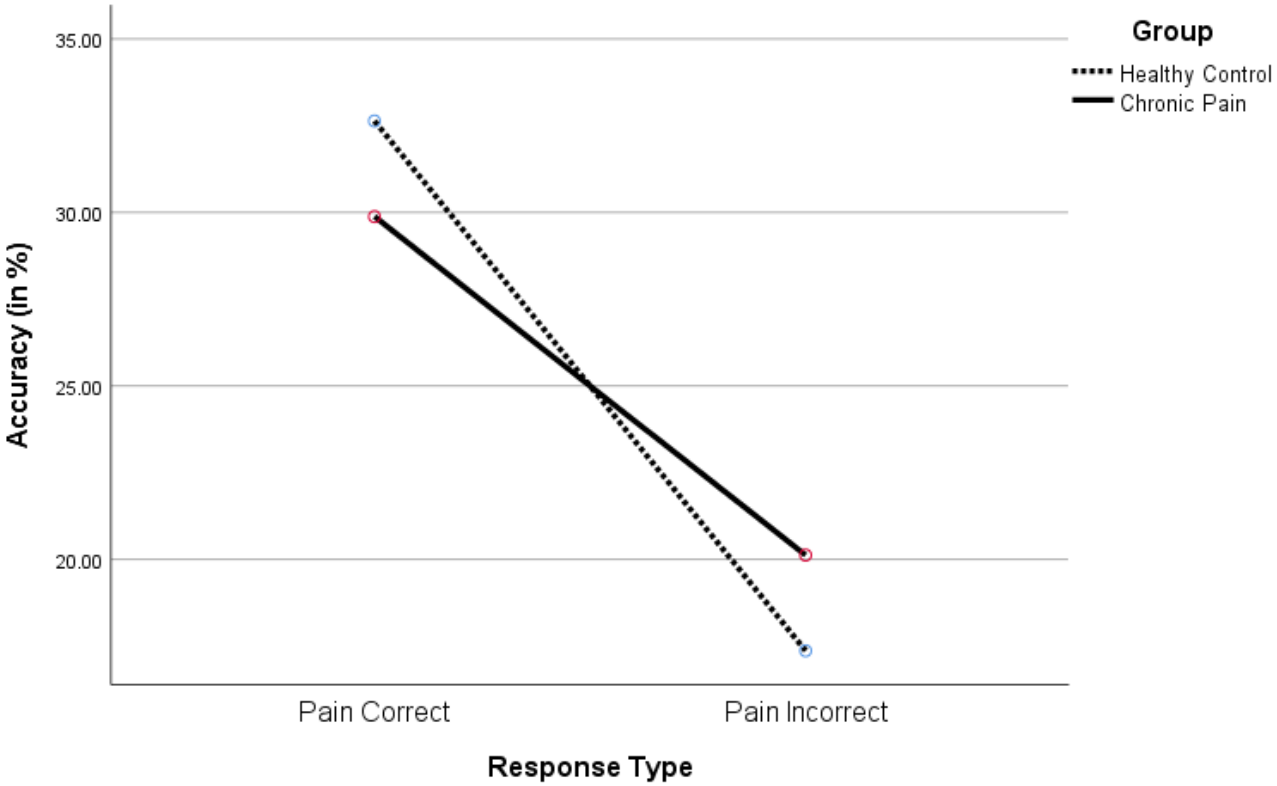


Figure 6.4: Accuracy (in %) by Group and Response Type.

Table 6.7: Mean (SD) Correct and Incorrect Recognition Scores for the Pain responses.

	Pain Correct Total	Pain Incorrect Total	Total
Chronic Pain	29.88 (7.46)	20.12 (7.46)	25 (8.89)
Non-pain controls	32.63 (5.24)	17.37 (5.24)	24.93 (10.96)
Total	31.23 (6.58)	18.77 (6.58)	

Additionally, in supplementary analyses, to investigate if there were any recognition differences in non-pain solutions generated in the IB task a 2 (Group, CP, NPC, between-subjects variable) x 2 (Response type; Non-pain correct, Non-pain incorrect, within-subjects variable) Factorial Mixed-Measures ANOVA was conducted to examine differences in recognition between the NPC and CP groups. Levene's test did not violate assumptions of homogeneity (p >.05). The analysis revealed a significant main effect of response type $F(1, 104) = 82.044$, p <.001, η^2 p = .441, such that there were significantly higher non-pain correct responses than non-pain incorrect responses. No significant main effect of group $F(1, 104) = 1.807$, $p = .182$, η^2 p = .017, nor an interaction effect was observed $F(1, 104) = .249$, $p = .619$, η^2 p = .002 (see **Table 6.8** for Mean/SD).

Table 6.8: Mean (SD) Correct and Incorrect Recognition Scores for the Non-Pain responses.

	Non-Pain Correct Total	Non-Pain Incorrect Total	Total
Chronic Pain	30.42 (6.46)	19.58 (6.46)	25 (8.42)
Non-pain controls	32.49 (9.93)	20.39 (10.60)	26.44 (11.88)
Total	31.43 (8.37)	19.98 (8.70)	

6.3.3.1 Supplementary Analysis: Comparing D-Prime (*d'*) and Criterion C (*C*).

To examine whether there were any group differences (CP, NPC) in *d'* an Independent Samples T-Test was performed using the Pain/Pain-illness (H and FA) *d'* scores. There was a significant difference in *d' t* (104) = 2.084, p = .04, *two-tailed*, such that the NPC group exhibited better discrimination ability and thus higher accuracy (M = .22, SD = .83), compared to the CP group (M = -.21, SD = .1.27). The magnitude in differences of the means (mean difference = .44, 95% *CI*: .02 - .85) was small (eta squared = .04). With respect to the Non-pain/Non-pain illness (H and FA) *d'* scores, no significant differences $t(104) = .260$, $p = .795$ were observed between the NPC (M = .03, SD = .96) and CP groups (M = -.02, SD = 1).

To examine whether there were any group differences (CP, NPC) in *C* an Independent Samples T Test was performed using the Pain/Pain-illness and Non-Pain/Non Pain-illness (H and FA) *C* scores. No significant differences in *C* were observed between the CP and NPC groups (all $p > .05$).

To sum, the D-Prime analyses revealed that participants in the NPC group exhibited better discrimination ability for Pain/Pain-illness solutions, than their CP counterparts. However, no differences were observed between the two groups for Non-Pain/Non-Pain illness solutions. No differences in *C* were observed.

6.3.4 Examining the relationship between Interpretation and Memory (Recall/Recognition) Biases

To investigate Hypothesis 4, that relationships would emerge between Interpretation and Memory biases (recall/recognition), a series of bivariate correlations were conducted between the IB, Recall Bias and Recognition Bias Pain/Pain-illness data for each group (CP, NPC). This identified significant correlations between several variables as shown in **Tables 6.9 and 6.10** below.

Chronic Pain Group

Table 6.9: Correlations between the IB (Pain, Non-Pain), Free Recall (Pain, Non-Pain) and Recognition (Pain H, M, FA, CR) data.

	IB Pain	IB Non-Pain	Free Recall Pain	Free Recall Non-Pain	Hits (H)	Misses (M)	False Alarms (FA)	Correct Rejections (CR)
IB Pain	1	**-.995** (*p* < .001)**	**.484** (*p* < .001)**	-.194 (*p* = .80)	-.202 (*p* = .072)	.202 (*p* = .072)	.142 (*p* = .153)	-.142 (*p* = .153)
IB Non-Pain		1	**-.478** (*p* < .001)**	-.197 (*p* = .076)	.202 (*p* = .071)	-.202 (*p* = .071)	-.127 (*p* = .180)	.127 (*p* = .180)
Free Recall Pain			1	**.238* (*p* = .041)**	-.022 (*p* = .437)	.022 (*p* = .437)	.176 (*p* = .101)	-.176 (*p* = .101)
Free Recall Non-Pain				1	.077 (*p* = .290)	-.077 (*p* = .290)	.013 (*p* = .464)	-.013 (*p* = .464)
Pain Hits					1	**-1.000** (*p* < .001)**	**.393** (*p* = .002)**	**-.393** (*p* = .002)**
Pain Misses						1	**-.393** (*p* = .002)**	**.393** (*p* = .002)**
Pain False Alarms							1	**-1.000** (*p* < .001)**
Pain Correct Rejections								1

* Significance p<.05

** Significance p<.001

Non-Pain Control Group

Table 6.10: Correlations between the IB (Pain, Non-Pain), Free Recall (Pain, Non-Pain) and Recognition (Pain H, M, FA, CR) data.

	IB Pain	IB Non-Pain	Free Recall Pain	Free Recall Non-Pain	Hits (H)	Misses (M)	False Alarms (FA)	Correct Rejections (CR)
IB Pain	1	**-.994** (*p* < .001)**	**.572** (*p* < .001)**	**-.520** (*p* < .001)**	-.224 (*p* = .055)	-.220 (*p* = .058)	-.021 (*p* = .442)	.027 (*p* = .425)
IB Non-Pain		1	**-.578** (*p* < .001)**	**.515** (*p* < .001)**	.230 (*p* = .055)	-.226 (*p* = .053)	.030 (*p* = .416)	-.036 (*p* = .401)
Free Recall Pain			1	-.082 (*p* = .282)	**-.263* (*p* = .030)**	**.270* (*p* = .026)**	-.002 (*p* = .495)	-.009 (*p* = .145)
Free Recall Non-Pain				1	-.043 (*p* = .380)	.052 (*p* = .358)	-.008 (*p* = .478)	-.006 (*p* = .483)
Pain Hits					1	**-.998** (*p* < .001)**	**.494** (*p* < .001)**	**-.496** (*p* < .001)**
Pain Misses						1	**-.495** (*p* < .001)**	**-.490** (*p* < .001)**
Pain False Alarms							1	**-.995** (*p* < .001)**
Pain Correct Rejections								1

* Significance p<.05

** Significance p<.001

6.3.4.1 Chronic Pain Group

There was a significant positive correlation between the Pain/Pain-illness IB data and the Pain/Pain-illness free recall data $r = .484$, $p < .001$, *one-tailed*. For the Non-Pain/Non-Pain illness IB data only a significant negative correlation between the Pain/Pain-illness free recall MB data was observed $r = -.478$, $p < .001$, *one-tailed.* Several correlations were also identified between the Pain/Pain-illness Recognition Data across the Hit, Miss, False Alarm and Correct Rejection category data (all $p < .05$). All other correlations between the IB, Recall Bias and Recognition Bias data were non-significant ($p > .05$).

Therefore, key results of this analysis were that as the number of Pain/Pain-illness solutions increased in the IB task, the number of Pain/Pain-illness solutions correctly recalled in the free recall MB task increased, while the number of Non-Pain/Non-Pain illness solutions decreased in the free recall MB task.

6.3.4.2 Non-Pain Control Group

There was a significant positive correlation between the Pain/Pain-Illness IB data and the Pain/Pain-illness free recall data $r = .572$, $p < .001$, *one-tailed*. For the Non-Pain/Non-Pain illness IB data there was a significant negative correlation with the Pain/Pain illness Free Recall data $r = -.578$, $p < .001$, *one-tailed*. A positive correlation was observed between the Non-Pain/Non-Pain illness IB data and the Non-Pain/Non-Pain Illness Free Recall MB data $r = .515$, $p < .001$, *one-tailed*. Several correlations were also identified between the Pain/Pain-illness Recognition MB Data across the H, M, FA, and CR category data (all $p < .05$). Notably, a significant negative correlation was observed between the Pain/Pain-illness Free Recall MB data and the percentage of Pain Hits in the recognition MB task, while a significant positive correlation was observed between the Pain/Pain-illness Free Recall MB data and the percentage of Pain Misses in the recognition task. All other correlations between the IB, Recall Bias and Recognition Bias data were non-significant ($p > .05$).

Like the CP group, key results of this analysis were that as the number of Pain/Pain-illness solutions increased in the IB task, the number of Pain/Pain-illness solutions correctly recalled in the free recall MB task increased, while the number of Non-Pain/Non-Pain illness solutions

decreased. Unlike the CP group, however, as the number of Non-Pain/Non-Pain illness solutions in the IB task increased, so too did the number of Non-Pain/Non-Pain illness solutions recalled. Conversely, as the number of Non-Pain/Non-Pain illness solutions in the IB task increased, the number of Pain/Pain-illness solutions recalled decreased. Finally, increased recall of pain-related words was associated with a reduction in the percentage of Hits and an increase in the percentage of Misses in the recognition MB task.

6.4 Discussion

6.4.1 Summary of findings

The aim of this study was to investigate interpretation and memory (recall and recognition) biases in a sample of chronic pain patients and non-pain controls. With respect to IB, no significant between-groups differences in the number of ambiguous scenarios interpreted as pain/pain-illness related were observed. Thus, in respect to hypothesis 1, the CP group did not interpret significantly more ambiguous scenarios in a pain/pain-illness related manner. As such there was a failure to reject the null hypothesis. With respect to recall memory, no significant differences in the number of pain/pain-illness solutions correctly recalled were observed between the CP and NPC groups. Consequently, with respect to hypothesis 2, the CP group did not recall more pain/pain-illness related solutions compared to their NPC counterparts, hence again there was a failure to reject the null hypothesis. In terms of recognition memory, while overall, participants recognised a higher percentage of pain/pain-illness solutions and non-pain/non-pain illness solutions correctly than incorrectly, an interaction was observed. That is, whilst both participant groups correctly recognised a higher percentage of pain/pain-illness solutions (and lower percentage of pain/pain-illness solutions incorrectly recognised), participants in the NPC group demonstrated a higher percentage of correct pain/pain-illness solutions and a lower percentage of incorrect pain/pain-illness solutions compared to the CP group. Added to this, supplementary analyses, including Pain/Pain-illness *d*' scores were significantly higher for the NPC group than the CP group,

indicating the NPC group possessed better discrimination ability between signal present/absent distributions and thus better overall recognition performance (i.e., higher accuracy). Thus, taken together these findings indicate that the CP group did not correctly recognise more pain/pain-illness related solutions generated in the ambiguous scenarios compared to their NPC counterparts, as such the null hypothesis could not be rejected.

Lastly, cross-bias correlational analyses (conducted as a function of group) revealed that for the CP group a significant positive relationship was observed between the number of pain/pain-illness solutions generated in the IB task and the number of pain/pain-illness solutions subsequently recalled. In the NPC group, a positive correlation was also found between the number of pain/pain-illness solutions generated in the IB task and the number of pain/pain-illness solutions subsequently recalled. That said, a notable difference in the correlational analyses emerged when comparing between the two groups. To expand, significant relationships between the Free Recall Non-Pain data and the Interpretation Bias data were exclusive to the NPC group. Firstly, as the number of scenarios interpreted in a pain/pain-illness manner increased, the number of non-pain/non-pain illness solutions recalled decreased. Secondly, as the number of scenarios interpreted in a non-pain/non-pain illness manner increased, the number of non-pain/non-pain illness solutions recalled also increased. Also exclusive to the NPC group were relationships between the free recall and recognition data. As the number of pain/pain-illness solutions recalled increased, the number of pain hits decreased, and pain misses increased. Thus, taken together, there was partial support for hypothesis 4 that relationships would emerge between Interpretation and Memory biases. Specifically, as the number of scenarios interpreted in a pain-related manner increased in the CP group, so too did the number of pain words correctly recalled. However, this finding was not unique to the CP group and extended to the NPC group. Further findings unique to the NPC group indicate differential processing of pain-related information between the CP and NPC groups.

6.4.2 Interpretation Bias

To recap, no significant differences were observed in the number of scenarios interpreted in a pain/pain-illness manner between the NPC and CP groups contradicting both previous research studies (Pincus et al., 1994, Pincus et al., 1996; McKellar et al., 2003) and recent meta-analytic evidence (Schoth & Liossi, 2016). The studies/meta-analysis presented previously reported evidence of adults with CP interpreting ambiguous information in a pain/pain-illness related fashion. The discrepancy between these findings and those of the present study may be due to the use of differing experimental paradigms. For example, the studies above measured IB using the Homographic/Homophonic Response Tasks which have been criticised for a lack of appropriate stimuli and response biases (Schoth & Liossi, 2017). Indeed, the meta-analysis conducted via Schoth and Liossi (2016) included studies employing the word-stem completion task; homographic response task; homophone task and the incidental learning task. In their meta-analysis they acknowledged several important methodological limitations, including those listed above, namely a lack of appropriate stimuli and response biases, and therefore called on future research to adopt more rigorous methodologies.

The AIBT used in the present study has previously been validated for use in adults (Gaffiero et al., 2022) and possesses higher ecological validity compared to paradigms such as the Homographic/Homophonic response tasks due to its free-response format. This enables participants to generate and provide their own solutions to each of the ambiguous scenarios presented, resulting in the solutions possessing a higher personal relevance. That said, the findings of the present study do not accord with previous studies using the AIBT in youth (Heathcote et al., 2017; Lau et al., 2019) or adult CP populations (Chan et al., 2020). However, it should be noted that these studies did not use a free-response format, and instead used a forced-choice response format. A key limitation of using a forced-choice response format is that when confronted with ambiguity, the solutions presented (often one pain/pain-illness related, one non-pain/non-pain illness related) may not reflect the participants own personal interpretation of the scenario. Hence, a forced-choice response format only provides a measure of researcher generated solution endorsement. Indeed, given that pain/pain-illness related words are used more frequently by

individuals with CP, this may explain why CP patients are more likely to endorse using the pain solutions presented. It is unknown whether if a free-response format were adopted in these studies participants with CP would initially interpret the ambiguous scenarios in a pain/pain-illness related fashion. Thus, one possible explanation for the discrepancy in AIBT findings may be due to differences in response format (i.e., forced-choice, free-response).

Of further consideration it should be noted that using this same task with healthy participants subjected to pain (cold-pressor) or no pain (warm water task) (Chapter 5), no significant differences in the number of ambiguous scenarios interpreted in a pain/pain-illness manner post a painful cold-pressor task were observed. Hence, research in the present thesis suggests that neither acute nor chronic pain influences interpretation bias, that said a fuller discussion of these findings will be presented in Chapter 7.

6.4.3 Memory Bias

With respect to recall bias, no significant differences in the number of pain/pain-illness solutions recalled between the CP and NPC groups were observed. According to Bower's (1981) Associative Network Theory, the pain solutions generated in the IB task should have activated a 'pain node' pertaining to memories for pain-related experiences in the CP group. Consequently, the threshold for pain-related information to enter consciousness would be reduced, increasing the frequency of pain node activation, resulting in more pain solutions being stored into memory. Hence, it would be expected that individuals with CP exhibit a recall bias for pain-related information. Consistent with this theory, Pincus and Morley (2001) provided evidence in their review of the literature that adults with CP exhibit enhanced recall for pain-related information. More recently, Schoth et al., (2019) also found evidence of a recall bias for sensory-pain words in a sample of participants with Chronic Headache. However, the present study contradicts the above theoretical predictions and research findings by observing no significant differences in free recall between the CP and NPC groups with respect to the number of pain/pain-illness solutions correctly recalled from the IB task.

Interestingly, this finding does accord with previous research by Karimi et al. (2016) who found that participants with Chronic Low Back Pain did not differ from Healthy Control (HC) participants in the recall of pain-related information, and Schoth et al. (2018) who found no evidence of a recall bias in patients with Chronic Headache. That said, a later study by Schoth et al. (2019) using the same experimental paradigm and population as in their 2018 study did find evidence of a free recall bias in individuals with Chronic Headache for sensory-pain words. Moreover, Busch (2007) found evidence of individuals with CP performing worse than their HC counterparts in a free recall task. The findings of Busch (2007) do accord with those reported in Chapter 5, in which participants allocated to the No Pain condition were found to correctly recall a higher percentage of pain/pain-illness than non-pain/non-pain illness solutions compared to their pain (cold-pressor) counterparts, but they do not accord with the present findings using a chronic pain group. Taken as a whole, these findings support the key conclusions of a recent systematic review and meta-analysis of the free recall literature, namely, that findings are mixed and inconclusive (Schoth et al., 2020).

The pattern of findings of the IB and Recall data are also consistent with the Recognition data. Contradicting previous research by Pincus et al. (1995), no evidence of enhanced recognition of the pain/pain-illness solutions was observed in the CP group. However, these findings are consistent with Flor et al. (1997) who observed no differences in the recognition of pain adjectives between CP and HC groups. D-prime (***d'***) revealed that in the present study, participants with CP performed worse than their HC counterparts in their discrimination of signal absent/present distributions for the pain words and thus overall poorer recognition performance. These findings are consistent with Grisart et al., (2007) who found recognition performance using a Remember/Know paradigm to be significantly poorer in CP patients than HC. Interestingly, they argued that the findings provided evidence of memory deficits in CP (as evidenced by global and objective measures of recognition, namely ***d'***). That said, they did acknowledge that while there may be impairments to certain aspects of recognition, the CP group were still able to report familiarity in that they knew something had been previously presented.

It should, nonetheless, be noted that a significant group by response type (pain correct vs. pain incorrect) interaction was observed. This revealed that participants in the NPC group obtained a higher percentage of pain correct, and a lower percentage of pain incorrect responses, than their CP counterparts. This suggests that there may be a processing difference in the CP group between the pain and non-pain solutions presented in the recognition task, which may account for their poorer performance compared to their NPC counterparts as indicated by ***d'***. This finding does add further credence to the notion that adults with CP display impaired recognition for pain-relevant stimuli (Flor et al., 1997; Grisart et al., 2007).

The notion that individuals with CP exhibit poorer recognition performance is in accordance with two explanations. These include the Attentional Cost Hypothesis (as outlined in Grisart et al., 2007) and Hypervigilance account (as outlined in Mazza et al., 2018). Briefly, the Attentional Cost Hypothesis proposes that the experience of pain captures attentional resources, leaving fewer resources available for concurrent cognitive processes. Accordingly, long-term memory retrieval (e.g., via recognition) is impaired due to less resources available for the encoding and storage of stimulus information. In the present study recognition memory was assessed after a one-month period, hence it can be argued impaired recognition performance may have occurred in the chronic pain group due to pain consuming limited attentional resources, adversely affecting the encoding and storage strength of the pain-related solutions generated in the ambiguous scenarios task. An alternative explanation that could explain the results is the Hypervigilance account. Briefly, it is proposed chronic pain patients demonstrate difficulties re-directing attentional and memory resources from pain-related sensations/thoughts/feelings, rejecting the notion of a reduction in attentional resources. Indeed, given the chronic pain group exhibited impaired recognition of the pain-related solutions generated in the ambiguous scenarios task, it is plausible that the interpretation of the scenario as pain-related and subsequent generation of a pain-related solution may have evoked threat/catastrophising with respect to their current on-going personal pain (not the task stimuli). As a result, attentional and memory resources were allocated to their on-going personal pain, thus impairing long-term memory retrieval of the pain solutions via recognition. These theories will be revisited in Chapter 7, when results both of this study and study 3 (Chapter 5) are discussed in combination. However, a critique of both theoretical

explanations outlined above is that while they provide intuitive explanations of the findings observed, it is not known whether such attentional cost and/or hypervigilance are vulnerability factors which increase the likelihood of developing chronic pain or are consequences of chronic pain. Additionally, the Integrated Functional Contextual Framework (Van Ryckeghem et al., 2019) emphasises the importance of contextual and motivational factors and how they shape cognitive biases, hence, understanding the causal mechanisms which impair recognition memory is likely to be more complicated than proposed by attentional cost and hypervigilance explanations.

To summarise, the above findings provide no evidence to support the notion that individuals with chronic pain display interpretation and memory biases (recall and recognition) favouring pain/pain-illness information. That said, there is evidence to suggest that pain impairs recognition memory. Despite the above findings leading to the rejection of the three main hypotheses, notable cross-bias findings were observed in supplementary analyses, which are discussed below.

6.4.4 Cross-Bias Findings: Interpretation, Recall and Recognition.

In the CP group a significant positive correlation was observed between the number of pain/pain-illness solutions generated in the IB task, and the number of pain/pain-illness solutions correctly recalled in the free recall task. A significant negative correlation was also found between the number of pain/pain-illness solutions generated in the IB task and the number of non-pain solutions correctly recalled in the free recall task. However, the direction of the relationships outlined above were also observed in the NPC group. Hence, these findings indicate similarities in information processing between the interpretation and recall paradigms. Indeed, such findings are consistent with Schoth et al. (2018) who observed correlations irrespective of group (Chronic Headache, Non-pain control) between the IB and Recall data. More specifically, as the number of interpretations made for sensory-pain words increased, so too did the number of sensory-pain words recalled. These findings suggest that cognitive biases do not exist independently but interact

and influence one another, with individuals more likely to recall pain-related information if it is interpreted as pain-related.

However, discrepancies in cross-bias correlations between the two groups were observed between the IB and free recall **non-pain** data. To expand, significant correlations between the free recall non-pain data and the interpretation bias data were exclusive to the **NPC group**. To recap, as the number of non-pain solutions recalled increased, the number of scenarios interpreted in a pain/pain-illness manner decreased. Likewise, as the number of non-pain solutions recalled increased, the number of scenarios interpreted in a non-pain/non-pain illness also increased. The drop in significance observed in the CP group suggest these individuals processed the non-pain/non-pain-illness solutions differently. In addition to the above, correlations between the free recall and recognition data were also exclusive to the **NPC group**, with increased recall of pain-related words associated with a reduction in the percentage of Hits and an increase in the percentage of Misses in the recognition MB task.

One possibility for the apparent processing differences observed above pertains to the notion of motivational relevance (Maratos & Pessoa, 2019). In the IB task participants were asked to generate their own personal solutions to the ambiguous scenarios presented, which were designed to be able to be interpreted in a pain/pain-illness or non-pain/non-pain illness related manner. Of the scenarios interpreted in a pain/pain-illness fashion and therefore a pain/pain-illness solution generated, these solutions are likely to be more motivationally relevant to those in the CP group due to their current experience of pain (Pincus & Morley, 2001; Uddin, 2015). Likewise, any non-pain/non-pain illness solutions generated are likely to be **not as** motivationally relevant to the CP patients, which may explain the lack of significance pertaining to the number of non-pain solutions generated in the IB task and the number of pain/non-pain solutions correctly recalled in the free recall task. Based on this logic, a lack of significance would not be expected in the NPC group, given that any pain/pain illness solutions generated would not be any more relevant than their non-pain/non-pain illness solutions. Indeed, that is exactly what the findings show, with the NPC group exhibiting no differences in the processing of the pain/non-pain solutions. Therefore, while between-groups differences may not have been observed with respect to the IB and recall

data in terms of the number of pain/pain-illness solutions generated and subsequently recalled, the above findings do suggest that those in the CP group processed scenarios interpreted in a pain/pain-illness manner differently than those interpreted in a non-pain/non-pain illness manner, which then subsequently affected processing (i.e., recall memory).

These findings also lend some support to Bower's (1981) Associative Network Theory in that the pain/pain-illness solutions generated in the IB task by participants in the CP group should be preferentially processed over the non-pain solutions, leading to increased recall of pain/pain-illness solutions. However, the mechanism of action by which this occurs remains unclear – whether this is the motivational relevance of the pain/pain-illness solutions activating a 'pain node' resulting in more pain solutions recalled in the free recall task is beyond the scope of the present study. However, the findings do accord with the key claims of the Integrated Functional Contextual Framework (Van Ryckeghem et al., 2020) that cognitive biases do not operate in isolation but interact with one another. This is observed via the significant correlations in the CP group between the number of pain/pain illness solutions generated in the IB task and the pain/pain-illness solutions correctly recalled in the Free Recall Task. These findings are not surprising, given that preferentially attending to one stimulus over another will result in enhanced encoding, and thus (likely) enhanced memory recall and recognition (Chun & Turn-Browne, 2007).

It is also important to note that only in the NPC group were correlations observed between the Recall and Recognition data. To recap, as the number of pain/pain-illness scenarios correctly recalled increased, the number of pain hits decreased, and pain misses increased in the recognition task. This could also potentially be explained by Motivational Relevance theory (Maratos & Pessoa, 2019). Over time, the pain-related solutions generated are no longer likely to be considered relevant to the participants in the NPC group, as in their life they are not suffering with chronic pain. As such, these solutions do not require any further in-depth processing beyond the initial free recall task. Hence, when presented with a recognition task including these solutions 1-month later, participants in the NPC group are much less likely to be able to discriminate between the pain solutions they had and had not used. This may be one potential explanation of why memory for these pain solutions may have decayed over time (as indicated by more misses and fewer hits).

6.4.5 Limitations

Several limitations of the present study should be considered. Firstly, while IB and MB was examined, attentional biases were not. Whilst this study was originally designed to measure AB using a free-viewing paradigm in conjunction with eye-tracking technology, due to the COVID-19 pandemic, the present study had to be modified for online-use. Thus, ABs were not measured due to data collection shifting from the laboratory to online. Indeed, because of the above, data collection for ***Chapter 6*** took place before ***Chapter 5***, thus a measure of pain sensitivity was not included, as the potential importance of this variable was not yet known. This, therefore, remains a key consideration for future research.

Secondly, the way in which individuals with CP process information may be dependent on the type of pain that they experience. For example, while studies have reported no evidence of cognitive bias(es) in CP samples (see Liossi et al., 2012), other studies have reported evidence of cognitive biases in specific CP samples (e.g., Chronic Headache, Schoth et al., 2018, 2019; Rheumatoid Arthritis, Sharpe et al., 2009). Thus, a limitation of the current study is that the CP group contained participants with a vast array of chronic pain conditions/diagnoses. This is argued to be problematic as the stimuli used in the tasks may lack relevance to the specific chronic pain condition the participants are suffering from, and thus the recruitment of mixed chronic pain samples in cognitive bias research has generally been recommended against (Van Ryckeghem et al., 2019). However, given that i) the IB task employed a free-response format so that participants could generate their ***own solutions*** to the ambiguous scenarios, ii) these solutions were the sole focus of the recall task, and that iii) a unique recognition task was designed for each individual participant with the 'Old' stimuli comprised their previous IB solutions, it can be argued that the stimuli did not lack relevance to the individual participants irrespective of their own pain condition.

Lastly, it is important to note that participants in the CP and NPC groups did differ on demographic variables including age, gender and the prevalence of mental health disorders (i.e., anxiety and depression). Given the online nature of the study, this was difficult to control for.

Matching CP and NPC participants on demographic variables including age/sex/mental health diagnoses would have been optimal, and therefore this serves as a limitation of the current study.

6.4.6 Future Research

The present study is the second to measure interpretation, recall and recognition biases in the context of a single study (for the first see Chapter 5), albeit the first in a chronic pain population. Given that the findings show participants in the CP group exhibited poorer recognition accuracy per se, and that in Chapter 5 a single instance of acute pain impaired memory accuracy for non-pain words, further research is needed to examine the causal factors associated with this. Additionally, research could employ differing retention periods to assess how recognition biases may change over time. In addition to the above, more research is needed measuring the three main forms of bias (AB, IB and MB) within the context of a single study. While this is a limitation of the present study, measuring each of these biases will help us to gain a more detailed insight as to how these biases influence and interact with one-another to impact pain chronicity. Relatedly, future research should attempt to measure these biases outside the laboratory. Given that laboratory studies are not sufficient to fully encapsulate the interrelated, dynamic and context-specific nature of cognitive biases, researchers should explore the use of other innovative technologies (e.g., Virtual Reality) and environments (Home Assessment) to assess information-processing in chronic pain patients' daily lives.

6.4.7 Conclusion

In conclusion, the present study found no evidence of biased interpretation or recall for pain/pain-illness stimuli. With respect to recognition memory, no between-groups differences in the percentage of pain/pain-illness solutions correctly recognised were observed – albeit an interaction effect was found demonstrating the NPC group (as compared to the CP group) obtained higher pain correct and lower pain incorrect responses. Supplementary analyses in the form of d-prime

revealed poorer recognition performance in the CP group, supporting the notion that pain impairs memory. Moving to the correlation analyses, cross-bias correlations were observed between the IB and Free Recall data for both groups independently, such that as the number of pain/pain-illness interpretations increased in the IB task so too did the number of pain/pain-illness solutions correctly recalled. This supports the general assumptions of the Integrated Functional Contextual Framework (Van Ryckeghem et al., 2019) that cognitive biases do not operate in isolation. Exclusive to the NPC group, however, were correlations between the IB (Pain/Pain-illness and Non-Pain/Non-Pain illness) and Non-Pain Free Recall data. These findings indicate a processing difference between the Pain/Pain-illness and Non-Pain/Non-Pain illness solutions among participants in the CP group, which map onto theories of motivational relevance. Lastly, correlations between the Free Recall and Recognition data were observed in the NPC group, such that as recall for Pain/Pain-illness solutions increased, the number of hits decreases, and misses increased. This provides evidence to suggest that in the NPC group the mental storage of pain-related information may have decayed over time, which again maps onto theories of motivational relevance. Taken together, all the above findings support the notion that cognitive biases do not operate in isolation but interact and influence one-another, and that individual's suffering with CP display impaired recognition for pain-related information per se.

Chapter 7 **Discussion**

7.1 Summary of Thesis Aims and Objectives

The evidence for cognitive biases, including attention, interpretation, and memory have been mixed. In recent years, theoretical models have been developed to guide future pain-related research. Notably, the Threat Interpretation Model (TIM, Todd et al., 2015) proposes that once information has been interpreted in a pain-related manner, the degree to which an attentional bias is observed is dependent on the perceived threat value of the stimulus (low, medium, high). Moreover, the Integrated Functional Contextual Framework (IFCF, Van Ryckeghem et al., 2019) challenges the common assumption that cognitive biases are intrinsically maladaptive, but instead highlights the importance of contextual and motivational factors that determine their functionality. Taken together, the TIM and IFCF helped to provide a framework for future pain-related research to investigate combined cognitive biases. This involves consideration of the contextual situations under which these biases appear (e.g., acute/chronic pain stage), and their underlying mechanisms of action (refer back to Chapter 1). Leading on from this, the aim of the current research was three-fold.

Firstly, to validate stimuli suitable for measuring pain-related attentional (***Study 1, reported in Chapter 3***) and interpretation (***Study 2, reported in Chapter 4***) biases in adults. Secondly, to examine whether the experience of pain influences attention, interpretation and memory biases in a pain versus no pain situation (***Study 3, reported in Chapter 5***). Thirdly, to examine whether individuals with chronic pain (CP) display interpretation and memory biases for pain-related information compared to non-pain control (NPC) participants (***Study 4, reported in Chapter 6***).

Study 1 validated pain-related images from three broad-topic databases (IAPS, GAPED, SPFD) and obtained ratings of their emotional properties (valence, arousal, threat value, pain intensity) to increase ecological validity and enable better investigation of attentional biases. ***Study 2*** developed and validated two stimulus sets suitable for the AIBT (Adult Interpretation Bias Task),

including a free response and forced choice stimulus set. Moreover, filler (i.e., neutral) scenarios were also validated to enable proper and rigorous investigation of adult interpretation biases. ***Study 3*** examined combined cognitive biases (attention, interpretation and memory) in a pain versus no pain situation to determine if: attention and interpretation biases are influenced by pain: if attention and/or interpretation biases influence the development of memory biases (including recall or recognition): if pain influences memory biases over time (immediately, or 1-month later) and finally, if there are any relationships between these three cognitive biases as a consequence of an acute pain experience. ***Study 4*** investigated interpretation and memory biases for pain-related information in adults with chronic pain and non-pain controls. Hence, taken together, studies 3 and 4 were designed to examine how pain (acute or chronic) influences cognitive biases.

7.2 Summary of findings

7.2.1 Study 1

64 healthy participants were asked to complete a validation task, whereby 105 images (45 pain, 60 neutral) obtained from 3 broad-topic databases (IAPS, GAPED, PICS) were rated according to four dimensions; pain intensity, threat value, valence and arousal. Analyses enabled the images to be categorised into varying degrees of pain intensity (neutral, low high) and threat value (low, medium, high). Thus, enabling in future research to test more specific predictions of key theoretical models (e.g., Threat Interpretation Model, Todd et al., 2015). This research also revealed that facial expressions depicting pain are generally rated as less threatening and of a lower pain intensity compared to pain images depicting physical injury – indicating that to induce high levels of threat and pain intensity, affective pain images, as opposed to facial expressions, are more suitable.

7.2.2 Study 2

241 participants were presented with a stimulus set comprising 62 scenarios (42 ambiguous, 20 neutral). Firstly, participants completed a Word Generation Task, whereby they were presented with the 62 scenarios individually and asked to type a response to complete the scenario using the first word(s) that came into their mind. Secondly, participants completed a Likelihood Ratings Task which involved re-presenting the 62 scenarios, accompanied with two researcher-generated solutions (one pain/pain-illness related, one non-pain/non-pain illness related). For the control scenarios two non-pain/non-pain illness solutions were presented. Here, participants were required to rate each solution according to their likelihood of usage to complete the ambiguous/control scenario from 0% to 100%. Analyses resulted in the development of a 'forced choice' ambiguous scenario set comprising 30 scenarios (18 ambiguous, 12 control) and a 'word generation' ambiguous scenario set comprising 32 scenarios (20 ambiguous, 12 control). Importantly, supplementary analyses revealed that adults reporting more recent pain experiences were significantly more likely to assign a higher likelihood rating to the pain/pain-illness solutions in the likelihood ratings task. This not only demonstrated ecological validity of the stimulus sets developed, but also provided preliminary evidence of a negative endorsement bias, with individuals who reported more recent pain experiences favouring the use of pain/illness-related solutions to complete the ambiguous scenarios.

7.2.3 Study 3

46 participants were randomly allocated to a pain (n = 22) or no pain (n = 24) condition. Interpretation and Attentional bias were measured via a 'free response' ambiguous scenario task and freeviewing eye-tracking task respectively. The pain images and ambiguous scenarios validated in ***Chapters 3 and 4*** were used as stimuli for these tasks. Interpretation and Attentional bias were measured both prior to and following a cold-pressor (pain condition) or warm water (non pain condition) task. To measure memory bias participants were first presented with a surprise free recall task during the in-person experimental session and were asked to recall as many solutions

that they could remember using to complete any of the two ambiguous scenarios tasks. Secondly, one-month later participants were asked to complete an online recognition task and identify which solutions they did (or did not) use to complete the ambiguous scenarios tasks. Thus, long-term memory was investigated using two retrieval methods (recall, recognition) with differing consolidation periods (recall – minimum, recognition – 1-month).

The findings of this study revealed that a single experience of pain is not sufficient to bias attention, interpretation and/or memory (recall and recognition). That said, irrespective of participant condition, attentional biases were observed for the High and Low Pain images (compared to neutral) with respect to indices of early and maintained attention, supporting the notion that attentional biases for pain-related information are ubiquitous (Blaisdale-Jones et al., 2021). Time course analyses also indicated that dwell time was significantly different during early and maintained attention for these image types. With individuals displaying initial vigilance and difficulty disengaging for High Pain images, and initial vigilance and disengagement for Low Pain images. Interestingly, it was found that participants in the no pain condition displayed a shorter latency to first fixation for the Low pain images post warm water task. Hence, suggesting that a potentially pleasant experience (warm water task) increases attention towards pain-related information (i.e., pain facial expressions). With respect to recall memory, participants in the pain condition correctly recalled a higher percentage of solutions post cold-pressor task. With respect to recognition memory, participants in the No Pain condition recognised a higher percentage of non-pain solutions compared to their Pain counterparts. These findings suggest that participants in the Pain condition displayed an advantage for the recall of solutions immediately following a painful experience, and the No Pain condition displayed an advantage for non-pain word memories (as measured by a recognition task) over the long-term (i.e., when assessed at 1-month).

Correlational analyses further revealed significant relationships between pain measures (obtained from participants in the pain condition) and cognitive biases post cold-pressor task for the acute pain group. As pain threshold decreased: the number of scenarios interperted in a pain/pain-illness manner increased; the number of pain/pain-illness words increased; and recognition for pain/pain-illness solutions one-month later also increased. Moreover, the total

fixation count for both high and low pain images also decreased. Additionally, as pain tolerance decreased, interpetation bias for pain/pain-illness increased and first fixation proportion for high pain images increased. Overall, these findings indicate that under conditions of acute pain these biases may perpetuate the pain experience in those individuals who are more sensitive to pain.

7.2.4 Study 4

153 participants comprising 77 with chronic pain (CP) and 76 non-pain controls (NPC) were asked to complete three tasks to measure interpretation and memory (i.e., recall and recognition) biases. Interpretation bias was assessed using a 'free response' ambiguous scenarios task. Here, 36 scenarios (18 ambiguous, 18 filler, as validated in ***Chapter 3***) were presented to participants individually. Memory biases were assessed using a surprise free recall task during the online experiment, and an online recognition task one-month later.

Results revealed no differences in the number of ambiguous scenarios interpreted in a pain/pain-illness or non-pain/non-pain illness manner. Thus, providing no evidence of a negative interpretation bias for the CP group contradicting previous research (Chan et al., 2020). Additionally, no between-groups differences were observed between the CP and NPC groups with respect to the number of pain/pain-illness or non-pain/non-pain illness solutions correctly recalled in the surprise free recall task. Thus, adding to the mixed literature surrounding recall biases in pain (Schoth et al., 2020). Lastly, analyses pertaining to the recognition data (arguably measuring long-term memory), showed that the NPC group obtained a higher percentage of pain correct and lower percentage of pain incorrect responses than their CP counterparts. Moreover, D-prime for the pain recognition data was significantly higher for the NPC group than the CP group. This suggested that NPCs possessed better discrimination ability and superior overall recognition performance. These findings are in accordance with two differing explanations, namely the Attentional Cost Hypothesis (see Grisart et al., 2007) and theories of Hypervigilance (Crombez et al., 2005; Veldhuijzen et al., 2006). Briefly, the attentional cost hypothesis proposes that the experience of pain consumes limited cognitive resources, leaving fewer cognitive resources

available for other concurrent cognitive processes. Consequently, the encoding of a stimulus, storage strength, and subsequent long-term memory retrieval (e.g., via recognition) are impaired. Given recognition was measured one-month later, according to the attentional cost hypothesis, encoding and storage strength would have been adversely impacted. Thus, the chronic pain group would be expected to display poorer discrimination ability and therefore poorer overall recognition performance as compared to the NPC counterparts. In contrast, in hypervigilance theory it is argued that chronic pain patients do not suffer from a reduction in attentional resources but tend to allocate them differently. Here, reduced cognitive performance observed in chronic pain patients is thought to be the result of difficulties re-directing attentional and memory resources from pain-related sensations/thoughts feelings. Given study 4 found recognition was impaired in the chronic pain group for pain-related words generated in an ambiguous scenarios task, it may be that the pain-related solution evoked threat/catastrophising in respect to their current on-going personal pain, with this (and not the task stimuli) capturing attentional and memory resources and thus impairing long-term memory retrieval via recognition.

Cross-bias correlations also revealed several important findings. Correlations between the interpretation bias and free recall data in the CP group showed that as the number of pain/pain-illness interpretations increased in the IB task, the number of pain/pain-illness solutions correctly recalled increased in the free recall task while the number of non-pain/non-pain illness solutions recalled decreased. The exact same findings were observed in the NPC group. However, in addition, for the NPC group a negative correlation between the number of pain/pain-illness solutions generated in the IB task and the number of non-pain/non-pain illness solutions correctly recalled in the free recall task was also found. Finally, exclusive to the NPC group was the finding that as the number of non-pain/non-pain-illness solutions generated in the IB task increased so too did the number of non-pain/non-pain solutions correctly recalled. Given these correlations were not observed in the CP group, there is some evidence to suggest that the CP group process scenarios interpreted in a pain/pain-illness manner differently than those interpreted in a non-pain/non-pain illness manner, which may then affect subsequent processing (i.e., recall memory).

7.3 Validating Stimuli Suitable for Measuring Attention and Interpretation Biases

The first key aim of this thesis was to develop stimulus sets suitable for measuring pain-related attention and interpretation biases in adults. This was achieved and the research reported in ***Chapters 3 and 4*** respectively. This section will provide a discussion of this research and findings, highlighting the importance of the studies and their individual contributions to the field of pain research.

7.3.1 Attentional Bias Stimulus Set

The evidence that adults display an AB for pain-related information is mixed (Schoth et al., 2010, 2015; Sharpe et al., 2009, Roelofs et al., 2003; Asmundson & Hadjistavropolos, 2007). Such evidence has led to questions surrounding the importance of AB to pain (Sharpe, 2014). Explanations to account for the conflicting findings have typically included methodological inconsistencies (see Dear et al., 2011), the use of less ecologically valid stimuli (i.e., words instead of pictures), and/or a lack of assessment of a stimulus' emotional properties which have been found to influence pain perception (Reicherts et al., 2013; Shaygan et al., 2017). Given the above, in the current research pain-related and neutral images from 3 broad-topic databases (IAPS, GAPED, PICS) were obtained and measurements of their emotional properties (i.e., valence, arousal, pain intensity, threat value) established. Importantly, threat value and pain intensity had not been previously measured for any pain-related pictorial stimuli, highlighting an original contribution of this study (presented in Chapter 3).

The stimulus ratings of the pain and neutral images revealed which stimuli scored higher/lower in valence and arousal and enabled the images to be split into three categories according to, not only their pain intensity (Neutral, Low, High), but also their threat value (Low, Medium, High). The categorisation of these images into varying degrees of threat value is important to test key theoretical predictions surrounding cognitive biases and pain. For example, the TIM (Todd et al., 2015) proposes differing attentional processes occur depending on the threat

value of a stimulus. Under conditions of sustained attention, the following attentional processes are predicted; low threat – easy disengagement of attention, medium threat – difficulty disengaging attention, high threat – attentional avoidance. Similarly, obtaining a measurement of pain intensity for these images is of equal importance given that it provides a measure of the sensory-pain dimension. To expand, the sensory-pain dimension refers to the intensity of the pain one experiences, including its spatial and temporal characteristics, and the quality of pain (Talbot et al., 2019). Typically, researchers only measure the valence of their stimuli, which in the case of pain images, does not reflect the affective-pain dimension. This is because the affective-pain component refers to the aspects of the pain experience that cause it to be unpleasant and aversive, and thus draws upon the affective-motivational aspects of pain (i.e., to take protective action). Whilst there has been considerable debate surrounding the degree to which these dimensions of pain are independent from one-another given these two dimensions are highly correlated (Fields, 1999), evidence suggests both dimensions are involved in the processing of pain-related images (e.g., facial expressions, see Kunz et al., 2012). Indeed, Villemure and Schweinhardt (2010) argue that it is important to include measures of both pain intensity and valence (i.e., sensory, and affective dimensions of pain) as while they may be sometimes closely related, unpleasantness can vary independently of pain intensity. Thus, an additional strength of the stimulus sets produced is that ratings pertaining to the sensory and affective dimensions of pain have been provided, which is not common in prior research which typically only includes ratings of valence and arousal.

That said, it should be noted that the measurement of arousal in the present study may not be considered optimal. The present study used a subjective measure of arousal (i.e., self-report), as opposed to an objective measure (e.g., measuring changes in heart rate, skin conductance or pupil dilation upon the presentation of each stimulus). However, given that arousal has both a physiological and subjective component – that is, how one reacts physiologically to the stimulus (unconscious) and how that stimulus is perceived (conscious), it could be suggested that including both a subjective and objective measure would have been optimal. This is because subjective measures offer a differing viewpoint than objective measures of arousal. Subjective measures allow the researcher to attempt to quantify the energy engendered from the viewpoint of an individual in relation to a stimulus (thus involving conscious cognitive processing), while objective

measures tap into the unconscious physiological responses to a stimulus (Ferreria & Saraiva, 2019). Therefore, in future research, using both objective physiological and subjective self-report data to measure arousal is recommended.

Irrespective of the debate concerning optimal capture of arousal in the present study, the images validated in this study provide clear implications for future pain-related attentional bias research. Namely, researchers can select stimuli in accordance with their own design needs and research questions, while avoiding issues associated with ecological validity, small stimulus set sizes and the failure to provide measurements of their emotional properties. Indeed, key theoretical predictions of the TIM can now be tested by utilising the developed stimulus sets with multiple categories of threat (**as was achieved in *Study 3 – Chapter 5)***. Taken together, study 1 provided stimulus sets suitable for measuring attentional bias in adults. Additionally, the stimulus sets validated in this study have provided the tools necessary for researchers to test the theoretical claims of the TIM (as achieved in Chapter 5), to gain a more detailed understanding of the complex attentional processes implicated in pain.

7.3.2 Interpretation Bias Stimulus Set

Unlike the AB literature, findings are generally consistent with the notion that both adolescents and adults with CP display a tendency to interpret ambiguous information in a pain and/or illness related manner (Pincus et al., 1994; McKellar et al., 2003; Schoth & Liossi, 2016; Heathcote et al., 2015, 2016; Lau et al., 2020; Chen et al., 2020). However, the traditional paradigms used to measure IB, and their ecological validity have been questioned. For example, traditional measures of IB including the Homographic/Homophonic Response Tasks as used by Pincus et al., (1994) and McKellar et al (2003), have been criticised for a lack of appropriate stimuli (Schoth & Liossi, 2017). To expand, the failure to control for differences in written and verbal frequency of use render homophones such as ‘Pain’ unsuitable, given that ‘Pane’ is an uncommonly used alternative. Thus, regardless of CP status, ‘Pain’ is likely to be the overwhelming interpretation participants provide, raising issues with the ecological validity of such experimental paradigms.

Limitations extend beyond direct measures of IB, however, with indirect measures, such as the Incidental Learning Task (Khatibi et al., 2014, 2015) also receiving criticism for the use of morphed facial expressions which are argued to lack ecological validity as they are less representative of 'true' facial expressions (Schoth & Liossi, 2017). Additionally, no studies have assessed the psychometric properties (i.e., internal consistency/test-retest reliability) of this Incidental Learning paradigm.

To provide a more ecologically valid measure of IB, Heathcote et al., (2015, 2016) developed the Adolescent Interpretation Bias Task (AIBT). Using this paradigm, Heathcote et al. found evidence for IB in adolescents reporting high levels of pain catastrophising and adolescents suffering with CP. Indeed, a key strength of this paradigm is that the ambiguous scenarios can be tailored to real-world situations thus being more applicable to the daily lives of participants. However, the paradigm developed by Heathcote et al. (2015, 2016) has two key limitations. Firstly, the AIBT uses a forced-choice response format, requiring participants to select one of two solutions (one pain/illness related, one non-pain/illness related) to complete each ambiguous scenario. This is problematic as the solutions presented may not actually reflect the initial interpretation that entered the participants' mind. Thus, it is unclear as to whether the findings of Heathcote et al., (2015, 2016) reflect a negative interpretation bias or are the result of the pain/illness solutions possessing higher personal relevance to adolescents worried about pain and/or suffering with chronic pain. Secondly, the AIBT does not incorporate filler (i.e., "neutral") scenarios. This is important as it helps to reduce the likelihood of biased responses via demand characteristics and priming (i.e., towards pain interpretations), which have been highlighted as problematic issues when using ambiguous scenarios in a previous review of IB paradigms (Schoth & Liossi, 2017). Hence, whilst the AIBT was a welcome step forward in the measurement of pain related IB, methodological modifications would increase the ecological validity of the paradigm even further.

Therefore, research conducted as part of this PhD entailed validating a set of ambiguous and filler scenarios using the AIBT in a population of adults but employing both free-response (Word Generation) and forced-choice (Likelihood Ratings) response formats. In accordance with

the aims of this study, two stimulus sets were developed, with one set for each response format. Moreover, control stimuli were also produced so that they could be randomly inserted amongst the ambiguous scenarios in future studies to reduce demand characteristics/response biases. Hence, this study (reported in Chapter 4) addressed the two main limitations of the original AIBT (Heathcote et al., 2015, 2016) by producing two sets of ambiguous scenarios, of which one can be used in a forced-choice response format and the other in a free response format. Thus, via this study a modified AIBT (suitable for adults) that possesses a higher ecological validity compared to its adolescent counterpart was produced. To the author's knowledge, this is the first stimulus set validated for use in adult populations that can be utilised in both free and forced choice ambiguous scenarios tasks.

Supplementary analyses of the Likelihood Ratings Data further revealed that adults who reported more recent pain experiences were significantly more likely to endorse using a pain/pain-illness interpretation in the Likelihood Ratings Task (i.e., Forced Choice), replicating the findings of previous research with adolescents (Heathcote et al., 2015; 2016, Lau et al., 2020) and adults (Chan et al., 2020). However, the extent to which this reflects an IB for pain/pain-illness information, or the pain/pain-illness solutions possessing a higher personal relevance is difficult to disentangle. Albeit the findings of the present study do accord with previous research reporting that negative interpretation bias was related to higher affective pain experiences (Keogh & Cochrane, 2002), and the findings of Heathcote et al., (2015), supporting the notion that pain catastrophising is a significant predictor of a negative IB in adolescents. Moreover, this study is the first to demonstrate that adults reporting more recent pain experiences endorse pain/pain-illness solutions for ambiguous scenarios. Thus, a clear future recommendation was that tasks employ the free response version of the AIBT, an approach that was adopted in Studies 3 and 4 (and reported in Chapters 5 and 6, respectively).

A further key strength of the free response ambiguous scenario set generated as part of the current PhD is its ability to be utilised in other novel task designs. A long-standing criticism of the pain and cognitive bias literature is the tendency for studies to only measure one form of cognitive bias, thus insight as to how cognitive biases may interact and/or influence one-another has been

lacking (Van Ryckeghem et al., 2019). Whilst research has begun to measure more than one bias within the context of a single study (e.g., Todd et al., 2016; Hughes et al., 2017; Schoth et al., 2018, 2019; Chan et al., 2020; Blaisdale-Jones et al., 2021), it is plausible to assume that factors including excessive task durations, participant fatigue, and a lack of ecologically valid paradigms may contribute to the hesitancy associated with measuring multiple cognitive biases within a single study. However, the adaptability of the ambiguous scenarios generated in Study 2 addresses each of these issues. To expand, the responses to the free response version of the AIBT (i.e., participant generated solutions) can be used as the stimuli in a variety of paradigms to measure other cognitive biases (as was achieved in Studies 3 and 4). For example, participants can be asked to recall any of the solutions they used to complete any of the ambiguous scenarios to provide a measure of recall bias or be presented with a recognition task containing their initial (i.e., Old) solutions and researcher-generated (i.e., New) solutions. The requirement of participants to generate their own solutions also means that the responses utilised in other tasks (such as those used to measure memory biases) are of direct relevance to the participant. Thus, they are relevant to the individual and therefore reduce issues associated with ecological validity. Taken together, study 2 provided stimulus sets suitable for measuring interpretation bias in adults (now published in Frontiers, Gaffiero et al., 2022). Additionally, the stimulus sets developed in this study have been used as a robust method to measure both interpretation and memory (recall and recognition) biases in studies 3 (Chapter 5) and 4 (Chapter 6). This highlights the adaptability and flexibility of the AIBT and, additionally demonstrates how ambiguous scenarios can be used in studies exploring combined cognitive biases in the field of pain.

7.4 Examining Combined Cognitive Biases in Acute and Chronic Pain Populations

The second key aim of the PhD programme of research was to examine whether the experience of pain influences attention, interpretation, and memory bias by investigating these cognitive biases in a healthy pain-free sample and ii) a pain-free sample subjected to acute pain. This aim was achieved in Study 3 (***Chapter 5***). The third and final aim of this thesis, was to investigate combined

cognitive biases in a chronic pain sample. This was achieved in study 4 (***Chapter 6***). This section will therefore discuss the key findings from these studies and highlight their importance and applications with reference to pain theory and research.

7.4.1 Attentional Bias

Cognitive biases have been identified in several differing forms of Psychopathology including both Anxiety and Depression, leading to the development of the Combined Cognitive Bias Hypothesis (CCBH, Everaert et al., 2014). Everaert et al. (2014) identified three differing categories of questions that stemmed from the CCBH. Including ***association*** questions -whether attention, interpretation and memory biases are interrelated. ***Causal*** questions **-** whether one form of bias influences subsequent biases or operate in parallel but independently of one another and ***predictive magnitude*** questions - using prospective research designs to observe the influence of single versus multiple cognitive biases on the course of depression. While such categories of questioning were initially derived with respect to the Depression literature, these question categories can be applied to cognitive bias research in the field of Pain. One example of a study addressing a predictive magnitude question comes from Lautenbacher et al. (2010) who employed a prospective design and found that an attentional bias towards positive words (as opposed to pain-related words) 1 day prior to surgery, was predictive of patients who subsequently experienced high pain intensity three and six-months post-surgery. Hence, the authors concluded that avoiding pain-related information increases the likelihood patients will develop chronic post-operative pain. This research demonstrated that attentional bias could influence the trajectory of acute pain becoming chronic pain.

At present, it remains unknown if these cognitive biases constitute vulnerability factors to the development of chronic pain or are the result of long-term exposure to pain, with the findings of Lautenbacher et al. (2010) suggesting the former. Cognitive-affective models of Chronic Pain assert that cognitive biases contribute to the mechanisms that influence the transition from acute to chronic pain. To recap, the Cognitive Affective Model (Eccleston & Crombez, 1999) proposes

several factors that moderate the interruptive nature of pain including pain intensity, novelty, predictability, threat and environmental factors (including emotional arousal and task difficulty). The Fear Avoidance Model of Pain (Vlaeyen & Linton, 2000) asserts that following a pain experience, high levels of pain-related fear result in the avoidance of physical activity which contribute to disease, disuse (physical decline) and depression. Consequently, the experience of negative affect and reduced pain threshold caused by disuse syndrome increases pain-related fear, resulting in the development of a maladaptive cycle that increases pain chronicity. Lastly, the Schema Enmeshment Model (Pincus & Morley, 2001) proposes that frequently repeated or continued experience of pain contributes to a process of enmeshment, whereby pain schema become entwined with illness and self-schema. The consequences of enmeshment include the maintenance and exacerbation of distress behaviour, with repeated pain experiences impeding major life goals which have negative ramifications for one's self-identity causing affective distress.

Considering the above, study 3 posed a causal question – does a single experience of pain influence attention, interpretation and memory biases? The aim of this study (reported in Chapter 5) was to understand the basic mechanism of how (or if) a painful experience influences cognitive biases, driven by the lack of research measuring cognitive biases both *prior to* and *after* a pain experience. The findings of this study indicated that a single experience of pain, without consideration of individual differences, is not sufficient to influence attention, interpretation and memory biases, which broadly suggests that maladaptive cognitive biases may be a consequence of repeated and/or long-term exposure to pain. Unfortunately, due to the ongoing COVID-19 pandemic, ABs could only be investigated in Study 3.

In recent years, considerable research effort has been dedicated to examining attentional biases in pain (for review see Crombez et al., 2013; Blaisdale-Jones et al., 2021). However, this area of research has been characterised by contradictory findings, which may be explained by considerable heterogeneity of the methodologies employed in various studies (e.g., differing experimental paradigms, stimulus section, participant samples etc.). Technological advancements over the past decade have contributed to the development of more accurate and reliable experimental paradigms, particularly the benefits of using eye-tracking technology. A previous

meta-analysis of studies employing the dot-probe detection task found attentional biases for pain words and pictures were exclusive to individuals suffering from chronic pain (Todd et al., 2018). However, more recent meta-analytic evidence comprised of studies using eye-tracking technology challenged this notion, concluding that attentional biases towards pain-related information are ubiquitous and independent of pain status (Blaisdale-Jones et al., 2021). The notion that attentional biases towards pain-related information are ubiquitous, accord with the eye-tracking findings of study 3. All participants, irrespective of pain manipulation, displayed biases in indices of early and maintained attention to both High and Low Pain images. Moreover, time course analyses also demonstrated that dwell time for High Pain compared to Neutral images was significantly greater between epochs 1-4 (0 to 2000ms) and 6 (2500 – 3000ms). Additionally, dwell time for Low Pain compared to Neutral images was significantly greater between epochs 1-4 (0 to 2000ms). Taken together, these findings suggest that all individuals (irrespective of pain condition and manipulation) demonstrate ABs to pain, highlighting the potency of pain-related information to interrupt and capture attentional resources.

Aside from the attentional bias findings of study 3 supporting recent meta-analytic evidence, they also support more traditional evolutionary explanations, including Motivational Relevance Theory (Maratos & Pessoa, 2019) and Cognitive-Affective Models of Pain (Eccleston & Crombez, 2007). Applied to Pain, evolutionary explanations propose that attentional biases are adaptive given they confer a survival advantage. For example, immediate awareness of a situation which has the potential to inflict bodily harm, enables an organism to generate a potentially protective response. Thus, attentional prioritisation of pain-related information should be ubiquitous. Motivational Relevance Theory (Maratos & Pessoa, 2019) adds a layer of complexity to traditional evolutionary explanations by specifying various factors which determine attentional prioritisation. Namely, stimulus saliency, task demands and cognitive and emotional states. According to this theory, attentional biases should be ubiquitous given the need to determine relevance. If a stimulus is deemed of relevance an appropriate protective response can be generated, particularly if there is potential for bodily harm. Considering the above, it is therefore not surprising that the eye-tracking analyses in Study 3 (and reported ***Chapter 5***) indicated the relevance of stimuli to be in the following order: High Pain, Low Pain, Neutral.

A key question that is logically raised from the above is, what purpose does attentional prioritisation serve in individuals with **chronic** pain? The answer here is simply none – the Integrated Functional Contextual Framework (Van Ryckeghem et al., 2019) holds the view that cognitive biases (including attention) are not inherently maladaptive, but instead the adaptive value of pain is determined by the context in which it occurs. Thus, in instances of acute injury (e.g., broken limb), accompanying pain and attentional prioritisation of pain serves to promote healing and prevent further injury. However, in instances of chronic pain, attentional prioritisation of pain-related information serves no purpose given that the pain cannot be escaped. Whilst Attentional Bias was not measured in study 4 due to the COVID-19 pandemic, these claims above are reflected in theoretical models of pain, including the Cognitive Affective Model (Eccleston & Crombez, 1999), Misdirected Problem-Solving Model (Eccleston & Crombez, 2007) and Motivational Account of Pain (Van Damme et al., 2010), which all highlight context and motivation as important factors that determine the utility of cognitive biases, and the impact of pain on the sufferer. For example, continuous experience of pain and subsequent interruption of attention may lead to pain-removal becoming a focal goal. Given there is no escape from pain, attempts to remove pain will inevitably fail, which contributes to increased distress, disability and impediment of life goals. Indeed, considering this logic, given study 3 employed a pain free sample, the finding that AB exists irrespective of pain manipulation is not surprising as AB is relevant to all individuals in such circumstances, due to its ability to facilitate a protective response to minimise bodily threat/harm and/or injury.

Threat has been identified as an important factor that influences attentional prioritisation. For example, it has been well documented that individuals who report being highly threatened by pain, subsequently over-attend to pain-related information (Boston & Sharpe, 2005). Study 3 used pain-related images validated in Study 1 to test the key theoretical predictions of the Threat Interpretation Model (TIM, Todd et al., 2015). To recap, this theoretical model proposes that the interpretation of a stimulus as pain-related and threatening determines whether a vigilance-avoidance pattern of processing is displayed. More specifically, attentional processes vary according to the perceived threat value of the stimulus; low threat leads to easy disengagement, moderate threat leads to difficulty disengaging, and high threat leads to attentional avoidance.

Study 3 provided some support for the TIM, with evidence of initial vigilance via High Pain images capturing a higher proportion of first fixations and the latency to first fixation for both High and Low Pain images being significantly shorter. With respect to maintained attention it was expected that the High Pain images would lead to attentional avoidance due to possessing a high threat value. However, findings indicated difficulty disengaging from the High Pain images, with this image type receiving a higher total number of fixations, and dwell time during early and maintained attention. The findings with respect to maintained attention are thus not consistent with the TIM, with the model predicting that moderate threat results in difficulty disengaging attention. Taken together, the findings of this PhD thesis provide partial support for the TIM, with Studies 1 and 3 combining to provide the first test of the theoretical claims of the TIM via manipulating multiple levels of stimulus threat.

Finally, the study 3 AB analyses did reveal an unexpected finding. Namely, that for the Low Pain vs. Neutral trials, participants allocated to the No Pain condition displayed a shorter latency to first fixation towards the Low Pain images post (vs pre) warm water task. These findings suggest that, surprisingly, a potentially pleasurable experience (warm water task) increases attentional allocation towards pain-related facial expressions. This appears counterintuitive, given theories of hedonic motivation. Briefly, such theories suggest that individuals are motivated to experience pleasure and avoid pain (Moen, 2016). However, it may be that a pleasurable experience maximises one's coping resources to confront pain-related stimuli. For example, previous research by Maratos and Sheffield (2022) examined whether engaging in brief Compassionate Focused Imagery (CFI) could improve pain coping. In their study, Saliva alpha-amylase (sAA) was taken at three-time periods; first, at baseline, second, during engagement with CFI or Control Imagery (of which participants were randomly allocated), and third, after participants were subjected to experimental pain (coincidentally, the same cold-pressor task, CPT). Results revealed that sAA (a measure of stress/pain) increased in response to the CPT for participants allocated to the Control Imagery condition only. Hence, the authors concluded that brief CFI was associated with dampened physiological responses to pain, and thus could potentially be a viable means of increasing pain coping. Whilst the Maratos and Sheffield (2022) study and study 3 of the current PhD research employed different designs, they are similar in that

they appear to suggest that a potentially pleasant experience (warm water task or CFI) may positively influence responses to pain. Indeed, this is further evidenced by the finding that avoiding the necessary confrontation of pain prior to surgery increases the likelihood of developing post-operative pain (Lautenbacher et al., 2010). Thus, these studies indicate that certain experiences related to AB could potentially improve pain coping – or direct attention to pain - when confrontation is necessary.

7.4.2 Interpretation Bias

Prior to study 2, no studies had validated ambiguous scenario stimuli suitable for measuring pain-related interpretation bias in adults. The findings of Study 2 (reported in Chapter 4) indicated that adults who reported more recent pain experiences were more likely to endorse pain/pain-illness related solutions in the Likelihood Ratings Task. These findings are consistent with previous studies examining IB in youth with and without chronic pain (Heathcote et al., 2015, 2016; Lau et al., 2019). However, a key criticism of studies measuring IB employing the Likelihood Ratings Task is that this task presents two researcher-generated solutions (i.e., one pain/pain-illness related, one non-pain/non-pain illness related), which may not reflect the participant's own personal interpretation of the ambiguous scenario. Hence, it is questionable as to whether this paradigm is an accurate measure of IB. Therefore, in studies 3 and 4, a Word Generation Task to measure IB was employed. Here, participants generate their own solutions to each ambiguous scenario using the first word (or words) that enter their mind, addressing the criticism that forced-choice response formats do not necessarily provide a true reflection of a participants' interpretation of ambiguous scenarios (refer to Chapter 2, Section 2.2.2.4). Taken together, the findings of these studies provided no evidence to suggest that adults with acute or chronic pain display an interpretation bias favouring pain/pain-illness related information.

To sum, therefore, these findings highlight a need to examine whether the observed discrepancy in findings between Study 2 and Studies 3 and 4 are a function of the IB task utilised. Indeed, a recent study by Chan et al. (2020) measured IB in adults with chronic pain and found

evidence of an endorsement bias favouring bodily-injury and long-term illness using a Likelihood Ratings Task. Hence, this adds further credence to the notion that the type of IB task deployed (word generation vs likelihood rating) may influence the results obtained. This stated, the findings of the present study are not consistent with a previous systematic review and meta-analysis conducted by Schoth and Liossi (2016), who concluded that individuals with CP favour pain/pain-illness related interpretations for ambiguous information, compared to controls.

One of the key questions that remains unanswered at present is whether IB precedes AB. As outlined in Chapter 1 (Section 1.3.6), the Threat Interpretation Model (Todd et al., 2015) proposes that IB precedes AB. However, Crombez et al. (2015) acknowledge that while IB may be a key driver of AB, IB may occur following attentional prioritisation of emotionally relevant stimuli. One way to assess whether IB precedes AB (or vice-versa) would be to counterbalance the order of task presentation (AB – IB, IB – AB). However, whilst technically possible, in Study 3, measuring AB via the inclusion of pain/injury-related images prior to IB, may inadvertently prime participants. Therefore, future research should attempt to assess AB and IB at multiple timepoints to examine their interaction and complex interplay.

7.4.3 Recall and Recognition Bias

Evidence suggests that pain-related material is more likely to be learned and subsequently retrieved (via recall and/or recognition) if it is consistent with the subjects prevailing experience. Indeed, according to classic theories of memory such as Craik and Lockhart's (1972) levels of processing it is predicted that the probability of subsequent recall and/or recognition is a direct function of the level of processing (shallow vs. deep). For the purposes of studies 3 and 4 it is arguable that the ambiguous scenarios task lends itself to deep processing, requiring participant to relate a solution they generate to an ambiguous scenario (which can be influenced by subjective experience – i.e., pain). Hence, according to this logic, the prediction that individuals with acute and chronic pain will exhibit enhanced recall and recognition for pain-related information is justified.

Unlike previous studies examining combined cognitive biases, studies 3 and 4 of this PhD measured both recall and recognition bias within the context of single studies. Recall and recognition memory both rely on long-term memory (Gillund & Shiffrin, 1984; Haist et al., 1992). Therefore, the key distinction between the measurement of recall and recognition biases in studies 3 and 4 is the period of consolidation. In the recall task the period of consolidation is minimal, whereas in the recognition task this is much greater (1-month). Recall and recognition memory provide different ways of retrieving information stored in long-term memory (i.e., recall – reproducing the stimulus items, recognition – responding 'yes' or 'no' to a cued stimulus). Hence, this provided a richer understanding of the impact of acute and chronic pain on long-term memory retrieval processes. Each of these long-term memory biases will be discussed in turn below.

With respect to recall bias, which was used to explore more immediate long-term memory retrieval, no between-groups differences in the number of pain/pain-illness solutions correctly recalled were observed in studies 3 and 4. However, study 3 did find an interaction effect between condition (pain, no pain) and manipulation (pre cold-pressor/warm water task, post cold-pressor/warm water task), such that participants in the pain condition correctly recalled a higher percentage of solutions post-cold-pressor task. These findings indicate that being subjected to acute pain makes immediate recall of information (whether that be pain-related or otherwise) better. Hence, further contradiction is added to the already existing mixed state of the recall bias literature – with the field marred by considerable variability in findings. To expand, a plethora of early studies reported evidence of a pain-related recall bias in individuals who repeatedly experience pain (Pearce et al., 1990; Edwards et al., 1992; Edwards & Pearce, 1994; Pincus & Morley, 2001). These findings accord with Bower's (1981) Associative Network Theory in that repeated activation of a 'pain node' reduces the threshold at which pain congruent materials is processed. In line with the above, the explanation offered for the study 3 results (reported in ***Chapter 5***) to explain the findings that a single experience of pain biased (enhanced) recall for both pain and neutral information, was that participants in the pain condition may have assigned greater priority to the scenarios generated post-cold-pressor task due to their increased personal relevance. Consequently, these scenarios (irrespective of being pain or non-pain related) were more likely to be encoded and subsequently recalled. However, in Study 4 a sample of chronic

pain sufferers were recruited, and no evidence for a pain-related recall bias was observed. Albeit this may be the result of internally versus externally generated stimuli. For individuals with chronic pain, internally generated stimuli (e.g., the persistent nature of pain) may capture attentional resources, meaning that externally generated stimuli (e.g., words generated as part of an interpretation bias task) are automatically assigned less priority and therefore have weakened memory traces resulting in no recall advantage being observed.

As mentioned above, conflicting findings are not uncommon amongst the recall bias literature. To expand, Busch (2006) reported that chronic pain patients exhibit impaired recall of pain-relevant stimuli. Here, cognitive avoidance was cited as the explanation, with chronic pain patients ignoring and distracting themselves from the pain-related stimuli. Indeed, more recent studies have corroborated the above findings, with Karimi et al. (2016) reporting that individuals with CLBP who exhibited a fear-avoidance response recalled significantly less pain than neutral words, supporting the initial explanation put forward by Busch (2006) regarding cognitive avoidance.

Considering the above, the present thesis provides no evidence to suggest that individuals with acute or chronic pain display a recall bias for pain-related information, which partially fits with Busch (2006) and Karimi et al. (2016). Moreover, in their review of the recall bias literature, Schoth et al. (2020) highlight that whilst there is some evidence of a recall bias favouring sensory-pain words (relative to neutral), the evidence for recall bias in adults with chronic pain is 'inconclusive'. That said, considerable heterogeneity in study design with respect to measuring recall bias appears to be a valid explanation for the mixed findings reported (see here also Chapter 2, section 2.3.1). Hence, future research employing more heterogenous task designs is needed to disentangle the currently mixed and inconclusive evidence of recall biases in pain.

Moving onto recognition biases it has been well documented that prior research examining recognition bias has been mixed (see Chapter 1, section 1.4.3) – with some research finding evidence to suggest that pain enhances recognition of pain and/or neutral stimuli (Schwarze et al., 2012; Wimmer & Buchel, 2015), and other research finding the exact opposite (Flor et al., 1997; Kuhadja et al., 2002; Grisart et al., 2007; Forkmann et al., 2016). The findings of study 3 (reported

in Chapter 5) indicate that participants in the non-pain condition were more likely to correctly identify 'old' non-pain words and correctly reject 'new' non-pain words, compared to their pain condition counterparts. Hence, this indicates an advantage for the recognition of non-pain words for participants in the non-pain group, albeit this was based on the pre cold-pressor/warm water task IB data. In study 4, however, it was found that pain impairs recognition memory. To expand, participants in the non-pain control group obtained a higher percentage of pain correct (and lower percentage of incorrect) responses than their chronic pain counterparts. Moreover, supplementary analyses revealed that pain/pain-illness *d'* scores were significantly higher for the non-pain control group than the chronic pain group. This indicates that the non-pain control group possessed better discrimination ability and overall recognition performance (higher accuracy). Thus, the findings of study 4 (reported in Chapter 6) suggest that the experience of chronic pain, only, impairs long-term memory retrieval via recognition.

It was predicted in studies 3 and 4 that the experience of pain (whether it be acute or chronic) would result in enhanced recognition of pain/pain-illness solutions generated in the Interpretation Bias tasks. Here, the pain solutions should become motivationally relevant given the congruence between the experience of pain and the valence of the solution (i.e., unpleasant). For example, previous research has illustrated a memory advantage for emotionally valanced experimental items (Grider & Malmberg, 2008). Given pain is highly unpleasant, there may be a shared mechanistic overlap with emotional memory (Gillam et al., 2020) given the experience of pain is highly unpleasant and thus could be interpreted as emotionally valenced (Vogt et al., 2019). Consequently, it would be plausible to assume that pain-related stimuli would exert similar memory effects compared to those observed with respect to emotional vs. neutral items. Indeed, Ferguson et al., (2007) found that high health anxious individuals recall and recognise health-related words more accurately and speedily. Thus, applied to pain it was assumed encoding and retrieval processes may be influenced favourably towards the pain solutions and therefore participants experiencing acute and chronic pain should exhibit enhanced recognition of pain/pain-illness solutions. However, it appears that the findings of both studies 3 and 4 do not support the notion of enhanced recognition of pain-related information. Indeed, study 4 provides evidence for

impaired recognition in chronic pain patients which will be explored via two competing explanations below.

Several explanations have been proposed to explain the cognitive (including memory) deficits observed in chronic pain patients (for review see Mazza et al., 2018). One explanation concerns the attentional cost of pain processing. The Attentional Cost Hypothesis (Vogt et al., 2019) argues that the experience of pain consumes a portion of attentional resources which are limited in capacity. Under certain circumstances pain captures and demands attention leaving fewer available cognitive resources to progress other/further tasks, subsequently negatively impacting task execution. Here, high levels of pain intensity (Eccleston, 1994), somatic awareness (Eccleston et al., 1997), and/or pain-related anxiety (McCracken & Iverson, 2001) result in priority processing of the pain experience to the detriment of the performance of ongoing tasks. Hence, applying the above explanation to the findings of study 4, it could be argued that the experience of pain consumes limited attentional resources, leaving fewer cognitive resources available for the encoding and binding of task-relevant information into long-term memory. Poorer recognition performance would therefore be observed 1-month later, due to the limited cognitive resources available during encoding causing the stimuli to have a weaker storage strength. As such, early-stage memory formation and subsequent recognition performance is adversely affected. This explanation is partially supported by the findings of Grisart et al., (2007). Grisart et al., argue that chronic pain exerts an attentional cost via a selective impact on attention demanding cognitive processes/resources. In their study, they distinguish between two forms of recognition: remembering and knowing, and claim that chronic pain impairs remembering (i.e., being consciously aware of having personally experienced something in the past), but not knowing (i.e., the feeling that one knows something has been previously presented). Consequently, the authors concluded that the remembering (but not knowing) impairment observed highlights the selective impact of chronic pain on attention-demanding cognitive processes.

Unlike the Attentional Cost Hypothesis, the Hypervigilance perspective (as outlined in Mazza et al., 2018) rejects the notion that individuals with chronic pain suffer from a reduction in attentional resources, but instead argues that these resources are allocated differently. Here,

chronic pain patients are thought to exhibit difficulty re-directing attentional and memory resources from their personal pain-related sensations/thoughts/feelings of which, subsequently, may account for reduced cognitive performance. Applied to the findings of study 4, it may be that the interpretation of ambiguous scenarios in a pain/pain-illness manner evoked threat/catastrophising, which meant attentional resources were directed to these personal feelings reducing resources that could be allocated to the encoding and storage of the pain/pain-illness stimuli, consequently impairing long-term memory retrieval via recognition one-month later. It is important to note that this theory, that chronic pain patients exhibit difficulty directing cognitive resources, shares some similarity with cognitive-affective models of pain, specifically the Integrated Functional Contextual Framework (Van Ryckeghem et al., 2019). In the IFCF it is argued that inflexibility/rigidity in attention, interpretation and memory contribute to negative pain outcomes. One explanation as to why such inflexibility may be observed in chronic (as opposed to acute) pain sufferers is that in these individuals (personal) pain removal is the focal goal (Eccleston & Crombez, 1999; Eccleston & Crombez, 2007; Van Damme et al., 2010). As such, attention is constantly captured by the pain experience which may be responsible for the common working memory and long-term memory deficits reported in the literature (Mazza et al., 2018). For example, this inflexibility might be caused initially by faulty central executive functions in working memory, specifically issues with inhibition and shifting of functions – which then later adversely impacts long-term memory retrieval (i.e., recognition).

In summation, the findings of studies 3 and 4 provide no evidence to suggest that individuals experiencing acute or chronic pain display enhanced recall and recognition for pain-related information. These findings suggest that the experience of acute and/or chronic pain does not enhance long-term memory retrieval for pain-relevant stimuli. However, the findings of study 4 do provide some evidence to suggest that chronic pain impairs recognition performance, and two contrasting explanations have been proposed to explain this finding.

7.4.4 Theoretical Implications and Cross-Bias Correlations

In ***Chapter 1*** (section 1.3.8) several key hypotheses were drawn from Cognitive-Affective models of Pain, including the prediction that cognitive biases will be associated with poorer pain outcomes. The findings of study 3 support this notion, with a lower pain threshold and/or shorter pain tolerance (i.e., greater pain sensitivity) correlating negatively with IB, AB and MB. To expand, as the time taken for participants to first report pain and/or remove their hand from the cold-pressor decreased, interpretation, recall and recognition of pain/pain-illness related information all increased. Moreover, individuals with a lower pain tolerance were also more likely to direct their first fixation on the High Pain images. Despite not being able to establish causation, the findings do support the general tenets of the Integrated Functional Contextual Framework (IFCF, Van Ryckeghem et al., 2019) theory that cognitive biases are interacting and inter-related. Most importantly, these findings suggest that pain sensitivity may influence pain-related cognitive biases, with individuals with higher pain sensitivity more susceptible to the potency of a painful experience. Considering this, an adapted model derived from the Threat Interpretation Model (Todd et al., 2016) is proposed built from the findings of Study 3, termed the Pain Sensitivity Model.

The Pain Sensitivity Model proposes that cognitive biases are influenced by one's pre-existing pain sensitivity (in the present research this was pain threshold and/or pain tolerance). Here, pain sensitivity is viewed as an individual difference variable that determines how an individual processes pain-related information. Moreover, pain sensitivity is argued to be a vulnerability factor, and therefore, a starting point to consider how pain may influence cognitive biases. Finally, it is important to note that attentional biases are considered ubiquitous due to their adaptive nature. Therefore, if a stimulus is interpreted as pain-relevant and threatening, all individuals, regardless of pain sensitivity, will display an attentional bias to pain/illness related information.

Much like the Integrated Functional Contextual Framework (Van Ryckeghem et al., 2019) the Pain Sensitivity Model holds the view that cognitive biases interact and influence one-another. However, in this new model, high pain sensitivity is associated with the increased allocation of

cognitive resources to pain-related information. According to this model, for individuals with high pain sensitivity, interpretation of a stimulus as pain-relevant and threatening (like the TIM, Todd et al., 2016), results in enhanced attentional allocation towards the stimulus. Alternatively, if a stimulus is interpreted as not pain-relevant and/or not threatening, normal attentional processing ensues. That said, the role of interpretation extends beyond initial ambiguity resolution, with interpretation able to influence attention following attentional prioritisation of the stimulus (consistent with Crombez et al., 2015). For example, if individuals with a high pain sensitivity interpret an ambiguous situation as pain-relevant and threatening, attentional resources will then be preferentially allocated to that stimulus. However, once attention has been allocated, an individual will constantly cognitively monitor whether the pain-related stimulus' perceived threat value has subsided, remains and/or has the potential to inflict bodily harm (enabling the individual to prepare a protective response). Hence, interpretation extends beyond the initial allocation of attentional resources and can operate via feedforward and feedback loops. Given the enhanced attentional allocation towards the stimulus, it is proposed that individuals with high pain sensitivity will exhibit enhanced encoding of pain-related material (as high pain sensitivity is regarded as a vulnerability factor), resulting in stronger storage in long-term memory. Consequently, high pain sensitive individuals exhibit enhanced long-term memory retrieval of pain-related material via recall and recognition processes. For example, recognition of a previously encountered painful stimulus in the current environment and/or recalling a painful situation when one's current experience is pain. This stated the combination of high pain sensitivity and attentional prioritisation of pain-related material may impair memory for non-pain related material. Indeed, previous studies have reported that in participants subjected to experimental pain encoding of non-pain words is attenuated as compared to their pain-free counterparts, suggesting that pain does not just influence the encoding of pain-related information but also impairs encoding of non-pain related information (Vogt et al., 2019).

Individuals with low pain sensitivity, on the other hand, exhibit increased flexibility in their cognitive processing of pain-related material. However, as mentioned previously, if a stimulus is interpreted as pain-related and threatening, attentional prioritisation will follow highlighting the ubiquitous and adaptive nature of attentional biases. Moreover, interpretation is still viewed to

occur beyond attentional prioritisation in low pain sensitive individuals, again, to determine whether a threat has subsided, remains and/or has the potential to inflict bodily harm (enabling the individual to prepare a protective response). However, considering that these individuals are less pain sensitive, they are hypothesised to exhibit increased flexibility in the way in which they attend to and encode (pain-related) information that is then stored into long-term memory. Consequently, the retrieval of both pain-related and non-pain related material remains intact (see **Figure 7.**1 below).

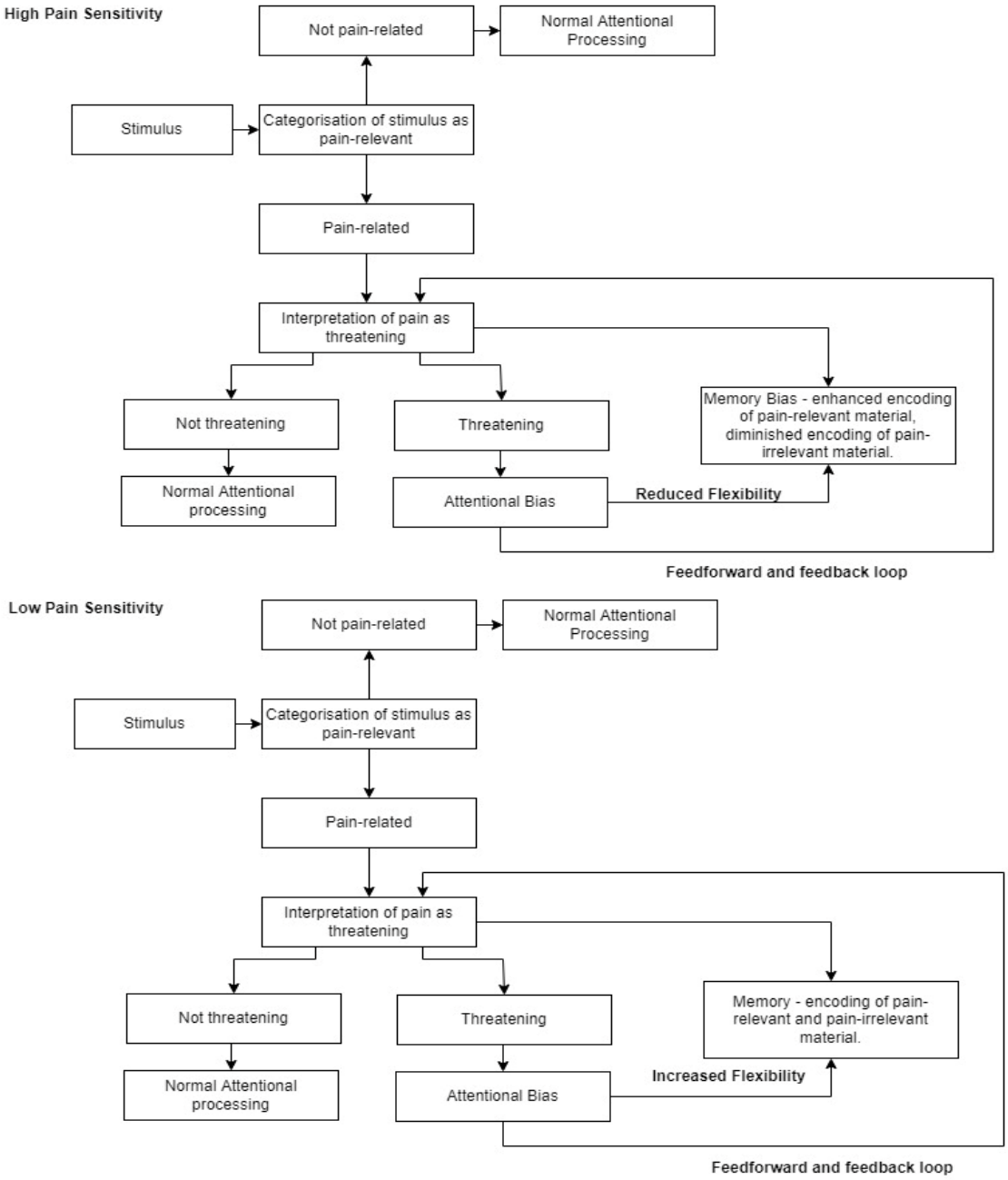


Figure 7.1: The Pain Sensitivity Model (adapted from the Threat Interpretation Model, Todd et al., 2015).

Indeed, it is important to re-state that the findings of study 4 suggest that individuals with chronic pain exhibited impaired recognition memory. Hence, it could be proposed that persistent pain may contribute to increased inflexibility in interpretation and attentional processing which then negatively impacts long-term memory retrieval processes. For example, as previously mentioned with respect to the Attentional Cost Hypothesis (Grisart et al., 2007) and Hypervigilance theories (Crombez et al., 2005; Veldhuijzen et al., 2006), the interruptive function of pain limits attentional resources, which then means individuals struggle to re-direct cognitive resources from their personal pain-related sensations/thoughts/feelings ultimately resulting in disrupted encoding and weaker memory storage. This consequently results in reduced cognitive performance, including impaired recall/recognition of pain-related and non-pain related information from long-term memory. To summarise, whilst the Pain Sensitivity Model requires rigorous testing and empirical validation, a key strength is that it is the first to actively integrate memory biases (recall and recognition) and acknowledge that, even in pain sufferers, individual differences are key in aetiology and pain progression/impairment.

Pain sensitivity, and individual differences in such, can also be mapped onto Motivational Relevance Theory (Maratos & Pessoa, 2019), in that it is important to view 'relevance' as a state-like variable that fluctuates across time. For example, study 4 identified an interesting pattern of cross-bias correlations. To expand, IB for pain/pain-illness solutions and recall of pain/pain illness solutions positively correlated in both the chronic pain (CP) and Non-pain control (NPC) groups. However, only in the NPC group were correlations observed with respect to IB and Recall for non-pain/non-pain illness solutions – indicating a processing difference in non-pain/non-pain illness solutions between the two groups. Also of note, was that a relationship between recall and recognition was only observed in the NPC group, such that increased recall of pain/pain-illness solutions was associated with decreased hits and increased misses in a recognition task presented one-month later. Taken together these findings are perhaps not unsurprising when considering Motivational Relevance Theory (Maratos & Pessoa, 2019). To expand, interpreting ambiguous information in a pain-related manner assigns the stimulus a higher relevance which may then lead to enhanced recall of such information. However, temporally the salience of these stimuli for the NPC group reduces over time, given they are not suffering with chronic pain – hence, there is no

need to allocate limited attentional resources to aid further in-depth processing. Because of reduced stimulus salience, the likelihood of memory traces for 'Old' pain/pain-illness stimuli existing are small for the NPC group, resulting in poorer recognition accuracy of such stimuli over time. Indeed, this appears a logical explanation of why memory for pain solutions decayed over time for the NPC group.

7.4.4.1 Attentional Cost versus Motivational Context – where do we go from here?

As mentioned previously in section 7.4.3, the Attentional Cost Hypothesis offers a logical framework via which the experience of pain may influence cognitive processes, including the allocation of attentional resources and how this constrains the resources available to be directed toward encoding and retrieval processes. This provides a suitable explanation for the findings observed in study 4 concerning recognition memory (Chapter 6). Indeed, considering pain captures and demands attention, it is no surprise that chronic pain patients often report that pain prevents them from having a clear mind, and conversely how pain-relief liberates this (Grisart et al., 2007).

Despite the above, conclusions that can be drawn from this thesis indicate that the impact of cognitive biases on individuals suffering from pain should also include one's motivational context. Relatedly, pain theories such as the Misdirected Problem-Solving Model (Eccleston & Crombez, 2007) propose that if pain-removal becomes a focal goal, this can fuel attentional biases towards pain-related information. For example, if individuals with chronic pain become motivated to adopt a biomedical problem frame, when there is no biomedical solution available, these concerted efforts to alleviate pain impede life goals and contribute to distress. A hypothesis which naturally emerges from this theory would be that individuals who accept their pain and focus efforts toward achieving their own personal goals, despite pain, may feel less threatened by pain, and less susceptible to cognitive biases. For example, consider two individuals, one of whom accepts their pain, adjusts their behaviour to manage it as best they can, and continues to pursue life goals; and another individual whom does not accept their pain, and is motivated to focus on pain-removal (despite no biomedical solution being available). It is likely that these differences in psychological flexibility (e.g., pain acceptance) and pain willingness (i.e., willingness to give up attempts to control or avoid pain) determines the extent to which pain interrupts their daily lives

(Probst et al., 2019). An individual who is motivated/focused on the removal of pain, is much more likely to be consumed by it physically and psychologically (ironic rebound), as compared to an individual who accepts their pain and the functional limitations it may pose. Indeed, evidence supports the notion that pain acceptance is a determinant of functional status and functional impairment (Esteve et al., 2007)

Similarly, attentional cost may depend on the extent to which pain sufferers allow themselves to be defined by their pain. For example, individuals who view themselves as more than the pain they experience, but nevertheless acknowledge and accept that pain is (and may continue to be) a persistent feature of their life, may experience less distress because while enmeshment between self, pain and illness schema still occurs, their self-worth is maintained given they do not view themselves as consumed by pain and illness to a significant degree. In contrast, individuals who focus exclusively on removing pain may be more likely to experience distress given the incongruency between the pain they experience and their sense of self. For example, refusing to accept that pain is impinging on their self-schema may result in the content of self-schema becoming trapped within pain and illness schema, particularly if multiple attempts to remove pain fail. Interestingly, recent research by Paschali et al., (2021) explored self-illness separation (which concerns the extent to which the illness one experiences defines, intrudes upon, or threatens the sense of self) in patients with fibromyalgia. The researchers found that a higher degree of enmeshment of the self-and-illness schema was associated with greater pain catastrophising, severity, interference, symptom impact and depression. Thus, acceptance of pain may serve as a psychological buffer that maintains self-illness separation in chronic pain patients, albeit this has yet to be investigated.

In short, understanding the motivational context via which an individual experiencing pain operates (e.g. acceptance vs. solution focused), can provide a more nuanced insight as to how cognitive processes may shape and influence behaviour. Thus, while attentional cost is intuitive and offers testable hypotheses, it would benefit from being incorporated within a wider theoretical framework that considers the role of differing motivational factors and context that are likely to shape, determine, and influence the potency of the cognitive biases experienced.

7.4.4.2 Individual Differences and Motivational Context – the future of pain and combined cognitive bias research.

Cognitive-affective models have been extremely influential in understanding how attention, interpretation and memory may influence the experience of pain, and how the experience of pain may also influence decision-making processes, the self-regulation of behaviour, and identity. The Threat Interpretation Model (Todd et al., 2015) and the more recently proposed Integrated Functional Contextual Framework (Van Ryckeghem et al., 2019) have been welcome additions to the field of pain. While the Threat Interpretation Model was designed to guide AB research, a key strength of the model was its testable predictions concerning the role of attention and interpretation bias in determining the type of attentional processing observed in individuals. For example, the interpretation of a stimulus as pain-relevant and highly threatening is predicted to lead to attentional avoidance. Hence, understanding how attention and interpretation biases may influence one another is important and has clinical implications for intervention (which will be described in more detail in section 7.5 below). The Integrated Functional Contextual Framework builds upon the Threat Interpretation Model by also actively considering memory bias. The notion that cognitive biases are functional, dynamic, and inter-related and/or interacting should be a key consideration of future studies investigating combined cognitive biases in pain. To expand, cognitive biases are not inherently maladaptive, but their adaptive value is determined by the context within which they operate. Understanding factors that may contribute to inflexibility/rigidity in the way individuals with pain attend to, interpret and remember pain-related information is of still upmost importance. This framework proposes that reduced executive functioning ability may be one cause of such inflexibility. However, research examining the causal factors which contribute to reduced executive functioning in chronic pain is scant and therefore also warrants further investigation.

A potential critique of the Pain Sensitivity Model outlined in section 7.4.4. is that it fails to consider motivational and contextual factors and is a simplistic model of individual differences. While pain sensitivity is undeniably an individual difference variable which forms the basis of this model, a broader perspective can be adopted to understand how pain sensitivity may operate under

differing motivational and contextual circumstances as specified by the Integrated Functional Contextual Framework (Van Ryckeghem et al., 2019). Much like genes and the environment shape human development, pain sensitivity, motivational and/or contextual factors may jointly shape the impact of cognitive biases on pain. For example, individuals with high levels of pain sensitivity may be more likely to exhibit attention, interpretation, and memory biases than their low pain sensitive counterparts. This could be a consequence of pain sensitivity negatively influencing executive functioning - reducing attentional control and one's ability to inhibit pain-related information, which may exacerbate the interruptive function of pain (as outlined in the Cognitive Affective Model, Eccleston & Crombez, 1999). Motivational factors may then determine the potency of the cognitive biases highly pain sensitive individual's experience. For instance, an individual who is highly sensitive to pain, may be more likely to adopt a biomedical problem frame whereby pain removal becomes the focal goal (as outlined in the Misdirected Problem-Solving Model (Eccleston & Crombez, 2007)). Repeated attempts and failure to remove pain may exacerbate cognitive biases through self-regulatory resource depletions. More specifically, an individual becomes less able to effectively regulate their thoughts, which means they are susceptible to pain-related attentional intrusions, reinforcing their interpretation of pain as an immediate threat that demands immediate action. The perseverance loop of individuals adopting a biomedical problem frame and seeking unavailable biomedical solutions may also have negative implications for identity. This continuous pursuit of an unachievable goal may prevent an individual from coming to terms with the impact of pain on their identity. Consequently, a greater degree of enmeshment may occur between the self and pain schema as individuals become consumed by seeking a solution to alleviate their pain. This emphasis on pain removal (as opposed to pain acceptance) may initiate an ironic rebound whereby the more effort one exerts to minimise their pain, the more they become defined by it (or in other words, the higher the level of enmeshment; as outlined in the Schema Enmeshment Model, Pincus & Morley, 2001). Alternatively, acceptance of pain would lead to a lower degree of enmeshment between the pain and self-schema, as individuals may be more likely to acknowledge that they are not consumed or defined by their pain, pain is and may always be a part of them, but their identity more than their pain.

It is clear from the above, that while the Pain Sensitivity Model can be viewed as a model of individual differences, it can also be tested within a broader motivational context. Therefore, future research should attempt to focus on both vulnerability and maintenance factors whilst also considering motivational contexts (e.g., a constant drive to seek a biomedical treatment) to gain a deeper understanding of the role of cognitive biases in the development and maintenance of chronic pain. Secondly, more prospective designs incorporating measures of pain sensitivity would be beneficial. For example, if individuals with high levels of pain sensitivity exhibit cognitive biases towards pain-related information, how does the experience of a pain influence these biases and/or subsequent behaviour? When pain cannot be removed, how might pain acceptance influence these cognitive biases? Does the acceptance of pain have ramifications for the level of enmeshment between self and illness schema? These are all questions that would be of benefit for future research to address. Finally, a key limitation of prior research and that of this PhD thesis is the reliance on exploring cognitive biases in a laboratory context. To gain a clearer understanding of the relationship between cognitive biases and pain, generating suitable measurement methods which can be implemented in the context of daily life (e.g., via home assessment or virtual reality) would help to gain insight as to how pain-related cognitive biases may operate in different contexts.

7.5 Clinical Relevance

Typically, interventions have attempted to target AB through Attentional Bias Modification (ABM). ABM training aims to target the tendency of chronic pain patients to selectively favour pain-related information by providing participants with a computerised training protocol designed to train participants to attend to neutral stimuli and avoid pain-related stimuli. The evidence for the effectiveness of ABM is mixed – with some studies reporting that ABM is not effective in improving CPT outcome and others that it is. For example, Bowler et al., (2016) used the dot-probe paradigm and manipulated stimulus duration (500ms or 1250ms) to retrain participants selective attention towards neutral, and away from, threat stimuli in an acute pain (vs. pain free) sample. Findings revealed that participants allocated to the Acute Pain group who received training

via dot-probe with a 500ms stimulus duration, showed increased pain threshold and tolerance compared to the control group. Hence, these findings indicate that ABM using short stimulus durations decrease pain sensitivity (i.e., increased pain threshold and tolerance). That said, Todd et al., (2016) examined the effects of single-session ABM training in healthy adults and found ABM did not affect attentional or interpretation bias. Moreover, Van Ryckeghem et al., (2018) also found no evidence that ABM is effective in improving pain-related outcomes. In their research, participants were assigned to an ABM (training away from pain) or sham (no training direction) condition. Participants completed a Random Interval Repetition task and cold-pressor task pre-and-post training. Here, using ABM to train attention away from pain was not found to result in better task performance when experiencing pain, or change participants level of attentional bias for pain. Such inconsistency has also been observed with respect to ABM in chronic pain patients, with studies reporting evidence to support the use of ABM for improving pain-related outcomes (Carelton et al., 2011) and others not (Heathcote et al., 2018).

In recent years, therefore, interventions have been designed to help individuals shift from a negative to positive interpretation style. An et al., (2020) developed an Interpretation Bias Modification for Pain (IMB-P) paradigm. Participants were randomly allocated to a training or control group. IB, AB and negative emotions were assessed before and after conducting IBM-P. Findings revealed that compared to the control group, chronic pain patients who received training displayed less of an IB favouring pain, reported fewer negative emotions, and with respect to AB, gazed at neutral words longer than previously unseen ('new') affective words. Hence, An et al., (2020) concluded that IBM-P can modify IB and subsequently effect AB and the prevalence of negative emotions, highlighting the potential clinical utility of such an intervention in pain management programmes. Considering the above, a key strength of the ambiguous scenarios developed in study 2 is that they can be integrated into a variety of experimental paradigms that can be used in CBM-I interventions to train participants to adopt a more positive interpretation style.

One notable consideration arising from study 3 (reported in chapter 5) is the potential role of pain sensitivity in influencing pain outcomes. Future research should aim to examine whether

those with high levels of pain sensitivity display cognitive biases (AB, IB, MB) for pain/pain-illness stimuli after being subjected to an acute pain experience. If pain sensitivity is found to moderate/mediate cognitive biases, then screening for pain sensitivity prior to painful procedures would enable healthcare settings to direct appropriate resources to aid recovery. Indeed, pain sensitivity may be a factor that influences whether an acute pain experience becomes chronic – which could then aid the development of preventative interventions.

Lastly, it is also important to note that the findings of study 4 suggest that pain may impair recognition memory. Memory complaints, particularly with respect to Working Memory and long-term memory dysfunction are well documented in the pain literature (for review see Mazza et al., 2018; Grisart & Van Der Linden, 2001). Indeed, an early study by McCracken and Iverson (2001) reported that of 275 chronic pain patients, 23.4% reported cognitive complaints pertaining to forgetfulness and 18.7% reported difficulties with attention. Mazza et al. (2018) reviewed the literature pertaining to chronic pain and memory and observed that chronic pain impairs attention-demanding memory processes. The authors argued that the inability to extinguish painful memory traces might represent one mechanism by which chronic pain persists after an initial injury has healed. Surprisingly, the programme of research presented within this PhD is the first to measure combined cognitive biases including both recall and recognition memory. Given the findings can be explained via Attentional Cost (fewer cognitive resources available negatively impacting task execution) and/or Hypervigilance (inflexibility in the allocation of cognitive resources), this opens the avenue for potential intervention to target reducing affective distress amongst chronic pain patients. For example, research suggests that chronic pain patients believe that memory impairment is an unavoidable side effect of medication use (Munoz & Esteve, 2005). Therefore, educating patients' regarding the potential causes of memory impairments, and designing new innovative interventions that aim to increase flexibility in attention and interpretation (and therefore memory), through the targeting and modification of multiple cognitive biases, may help to improve pain coping and pain outcomes.

7.6 Limitations

Although four novel studies were presented as this PhD programme of research, it should be observed that they were not without limitations. These are expanded upon below.

7.6.1 Can external stimuli represent an internal experience?

A critique that could be levied at each of the studies presented in this PhD thesis concerns the extent to which external stimuli (e.g., the use of pain/injury related images and words) can represent an internal experience (i.e., pain). However, given pain is a subjective private experience, external stimuli are useful in that they offer an indirect way to assess how an individual may make sense of, or respond behaviourally, to their internal experience of pain. For example, individuals who experience pain often ruminate about pain, which involves negative inner thoughts, reflecting their internal experience. It could be argued that words facilitate understanding and explanation of how things relate to one another (e.g., my pain feels like a stabbing sensation), while images on the other hand, denote realities of the internal experience (e.g., grimacing facial expression due to chronic headache). Indeed, evidence suggests that when stimuli (particularly images) are of a higher personal relevance to the pain sample under investigation, cognitive biases (e.g., attention towards pain) are more likely to be detected (Dear et al., 2011; Schoth and Liossi., 2013). Therefore, while external stimuli cannot fully represent an individual's internal experience, they do provide an indirect insight into one's subjective experience of pain and is thus a key reason why words and images were validated and used to measure cognitive biases in this PhD thesis.

7.6.2 Study 1

While Study 1 succeeded in validating a stimulus set suitable for measuring pain-related attentional biases there are a couple of important limitations to consider. Firstly, there was no assessment of test-retest reliability – it would have been beneficial to establish whether normative ratings

pertaining to valence, arousal, threat value and pain intensity were consistent over time. Secondly, it is also important to consider whether arousal can be sufficiently captured via self-report. In the present study participants were asked to rate each image according to the question 'How strongly does this image make you feel'? It can be argued that also including an objective measure of arousal via physiological measures (heart rate variability, pupil dilation or electrodermal activity) may be optimal in future AB research. Including both measurements in future research would capture objective physiological responses and subjective feeling responses of arousal (Scherer, 2001).

7.6.3 Study 2

One notable limitation of the ambiguous scenarios is that while they were designed with respect to valence orientation (i.e., negative vs. neutral), they do not consider adaptiveness in relation to context (Mehu and Scherer, 2015; Van Ryckeghem et al., 2019). That is, interpretation patterns differ in their adaptiveness depending on whether an individual is suffering from acute or chronic pain. Moreover, considering the distinction between anticipation (i.e., preventing immediate bodily harm) and attribution (i.e., implications of chronic pain) would have also been beneficial in increasing the ecological validity of the stimulus set. To expand, anticipating and/or avoiding events/situations where potential bodily injury is a possibility would be considered adaptive. However, appraising a medically explained, persistent pain as immediately threatening subsequently fuelling fear and avoidance of physical activity, would be relatively less adaptive. Hence, anticipation and attribution appear to also be a key distinction that may also influence interpretation biases in acute and chronic pain populations. This potentially serves a limitation of ***Study 2***, but also ***all*** previous pain related IB research. Future ambiguous scenario stimulus sets could therefore be designed and validated to consider rigidity/adaptiveness.

A second limitation of ***Study 2*** was that, in short, there is no objective means to assess whether a participant uses their initial interpretation when confronted with ambiguity. Hence, consciously (or unconsciously) participants may modify their initial interpretation. The study actively

attempted to minimise this via asking participants to generate the "***first*** word (or words) that came into their mind". Of note, this is criticism that can levied at interpretation bias methodology per se, and attempts were made to address this in the present study by the clear instructions provided.

7.6.4 Study 3

Previous studies have highlighted the utility in counterbalancing the order of AB/IB tasks to examine the interplay between each cognitive bias (Crombez et al., 2015). Therefore, a limitation of ***Study 3*** pertains to the inability to assess whether AB precedes IB (or vice versa). While all other aspects of the study were counterbalanced, the IB task was always presented before the AB task to circumvent priming (i.e., pain images may prime pain-related interpretations), and thus actually serves as a strength of this study. Secondly, whilst this study took a step forward in measuring cognitive biases before and after a pain or no-pain situation, assessing cognitive biases over multiple durations would also enable examination of how cognitive biases change over time. This should therefore be a priority of future pain-related combined cognitive bias studies. Finally, it is important to note that this study was underpowered. Opportunity sample recruitment resulted in 46 participants (students) from the University of Derby taking part in the research. Whilst this is fewer than suggested by the power analysis, participant sample size did exceed that of previous combined cognitive bias research (e.g., Schoth et al., 2018: $n = 37$).

7.6.5 Study 4

Due to circumstances beyond the researcher's control, Study 4 did not include a measure of pain sensitivity or attentional bias. Originally, this study was due to take place in person, however, due to the COVID-19 pandemic and the vulnerable nature of the participants, the study was repurposed for online data collection. This had a knock-on effect in that it was difficult to control for demographic variables pertaining to the sample recruited. Indeed, given Study 4 was conducted prior to Study 3, the findings indicating that pain sensitivity may be an important variable to

include in future research were not yet known. Hence, a logical next step for future research would be to measure each of the combined cognitive biases (including recognition memory) in a chronic pain sample, but also to include a measure of pain sensitivity, to investigate the extent to which pain sensitivity influences cognitive processing of pain-related information in both pain sufferers and when non-pain controls are subjected to a pain or no-pain situation.

7.7 Conclusion

Taken together, the four studies presented within the scope of this PhD thesis can be summarised as follows. Studies 1 and 2 validated stimulus sets suitable for measuring pain-related attention and interpretation biases. Study 2 also found that adults reporting more recent pain experiences were more likely to endorse using a pain/pain-illness solution to complete the ambiguous scenarios in forced-choice situations. Study 3 represented the first study to measure combined cognitive biases (including both recall and recognition memory) prior to and following a pain or no-pain situation. The findings of this study indicated that a single experience of pain is not sufficient to influence cognitive biases. That said, correlational analyses revealed relationships between cognitive biases and pain threshold and tolerance, suggesting that pain sensitivity may be an important variable that mediates/moderates cognitive biases. Study 4 was the first to measure interpretation and memory (recall and recognition) bias in a chronic pain (vs. non-pain control) sample. No evidence of interpretation, recall or recognition bias was observed. However, with respect to recognition memory the chronic pain group exhibited lower accuracy and discrimination ability, suggesting that pain may impair long-term recognition accuracy. Correlational analyses also revealed that for participants in the non-pain control group an increase in the recall of pain/pain-illness solutions was associated with an increase in misses and decrease in hits with respect to recognising pain/pain-illness solutions one-month later. This finding supports the notion that memory for pain-related information in non-pain controls decays over time. Considering the findings of the four studies presented within this PhD thesis a new model of pain (based on the Threat Interpretation Model, Todd et al., 2015) – the Pain Sensitivity Model - is presented.

Moreover, suggestions for future research include not only testing the model with experimental and chronic pain participants but also developing interventions that aim to target multiple cognitive biases. Overall, this PhD thesis achieved each of the three key aims outlined in Chapter 1 (section 1.7) and as highlighted in this conclusion, provides an original contribution of knowledge to the field of Pain via theory advancements, future research directions and findings of clinical relevance.

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