THE ASSOCIATION BETWEEN ADULT ATTACHMENT STYLE AND PAIN PERCEPTION IN A SOUTH AFRICAN COHORT

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A Thesis submitted to the Faculty of Health Sciences, University of the Witwatersrand, Johannesburg, in fulfilment of the requirements for the degree of PhD (Physiology).

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DECLARATION

I Gabriella Elisabeth Stamp declare that this Thesis is my own, unaided work. It is being submitted for the Degree of PhD (Physiology) at the University of the Witwatersrand, Johannesburg. It has not been submitted before for any degree or examination at any other University.

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(Signature of candidate)

_____25_________day of____January_____2024 in___Johannesburg___________

PRESENTATIONS ARISING FROM THIS PROJECT

Event/conference	Title of presentation	Date
Presentation at the Brain Function Research Group's annual research day (Johannesburg)	Associations between adult attachment and chronic pain in a South African population	14/09/2022
2023 PainSA congress (Johannesburg)	Plenary talk: Attachment styles and pain Free session presentation: Adult attachment style is associated with prevalence but not burden of chronic pain in a national sample of South Africans	05/05/2023 – 07/05/2023
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ABSTRACT

Our response to threats, including pain, is believed to be learnt during our early interpersonal connections and experiences. Interpersonal relationships can be measured through four adult attachment style classifications: Secure, Dismissing, Preoccupied and Fearful, with the latter three being collectively classified as Insecure attachment styles. Preliminary epidemiological evidence suggests that Insecure attachment styles are more prevalent in those with chronic pain, while experimental studies investigating the association between adult attachment and pain are inconclusive. In two separate investigations, the aims of my research were (i) to determine the association between adult attachment style and chronic pain prevalence and burden in a South African population, and (ii) to determine the association between the different adult attachment styles and measures of experimental pain as a way of assessing a potential mechanism for possible differences in pain perception between the attachment styles. In the first study, a nationwide online survey of a general South African population assessed adult attachment style (using The Experience in Close Relationships - Relationship Structures (ECR-RS) Questionnaire), prevalence of chronic pain and psychological factors that are typically associated with pain, including depression, anxiety and pain catastrophising. In participants who reported experiencing chronic pain, the association with attachment style and pain burden (pain sites, severity and interference, using the Brief Pain Inventory) was further investigated. A total of 2371 participants completed the survey, with the cohort being generally young in age (median age 23 years; IQR 20-28), well-educated and primarily female (74%), with predominantly a middle-to-high socioeconomic status. In this cohort, I found a higher-than-expected prevalence of chronic pain (27%); previously reported prevalence data in a South African population found the prevalence to be 18%. All three Insecure attachment styles were associated with increased chronic pain prevalence when compared to the Secure attachment style (Dismissing: 31%, Odds ratio [95%CI] = 1.38 [1.02-1.85], $p=0.037$; Preoccupied: 42%, Odds ratio [95%CI] = 2.26 [1.62-3.13], $p<0.001$; Fearful: 49%, Odds ratio [95%CI] = 2.95 [2.03-4.29], $p<0.001$). In participants with chronic pain, adult attachment style was not directly associated with the overall burden of chronic pain.

Rather, my study found that pain catastrophising was the mediating factor between Insecure adult attachment styles and an increased burden of chronic pain.

Female volunteers who had completed the survey were invited to participate in the second study, which involved in-person experimental procedures to evaluate the experience of thermal pain and mechanisms of pain analgesia using the Conditioned Pain Modulation (CPM) paradigm. In the 103 young (median age 21 years; IQR 20-23) and well-educated (all completed at least secondary education) sample, no significant relationship was found between attachment style and heat pain threshold ($t(54) = -0.45$, $p = 0.654$), heat pain tolerance ($t(47) = -1.16$, $p = 0.250$), and intensity of heat pain (Estimate [95%CI] = -0.11 [-0.34-0.11], p-value = 0.330). Similarly, descending pain inhibition (assessed using CPM) was not associated with adult attachment style ($t(59) = -0.97$, $p = 0.338$).

In these South African cohorts, adult attachment style directly associated with chronic pain prevalence, with remarkably more than double the chronic pain prevalence in Fearfully, compared to Securely, attached individuals. A possible mechanism underlying the association between insecure attachment style and high chronic pain prevalence may be differences in pain modulatory pathways, which was investigated through the CPM test paradigm in Part 2 of my research. Pain catastrophising mediated the relationships between attachment style and burden of pain, highlighting the role and impact of cognitive factors and the perception of threat on both attachment style and pain. Adult attachment style did not associate with perception of experimental pain, nor did it associate with mechanisms of pain inhibition. The data of the two research components of my thesis highlight the differences between chronic clinical pain and the once-off experience of experimental pain in a controlled and safe environment. The negative data in the experimental study may be explained by three main limitations: (i) The experimental protocol was not threatening enough and was unlikely to consistently activate the adult attachment system; (ii) individuals with high attachment anxiety and attachment avoidance dimension scores did not participate in the experimental study, which means the sample was biased and may not have shown any differences even if the protocol was threatening enough to activate the attachment system; (iii) the experimental pain protocol likely does not capture the threatening nature of chronic pain due to complex interactions of psychosocial factors that accompany chronic pain. These limitations are informative for future experimental pain studies, and I believe that CPM cannot, at this point, be ruled out as a mechanism for the increased chronic pain prevalence in insecurely compared to securely attached individuals. Moreover, pain catastrophising as a potential mechanism underlying the association between adult attachment style and the prevalence of chronic pain may also be a potential avenue for future studies to pursue.

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Lastly, my deepest thanks go to my friends and family for their unwavering love and support. A special mention to my parents Ingrid and Alex, my brother Jason, and, of course, to Nicholas — your belief in me has been my strength and your constant support and love have been my anchor throughout this journey. I love and appreciate you all immensely.

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LIST OF ABBREVIATIONS

ACC: Anterior cingulate cortex

AUC: Area under the curve

BPI-sf: Brief Pain Inventory – short form

CI: Confidence interval

CPM: Conditioned pain modulation

DASS-21: Depression, Anxiety and Stress Scale 21

dlPFC: Dorsolateral prefrontal cortex

DNIC: Diffuse noxious inhibitory control

ECR-RS: Experience in Close Relationships - Relationship Structures

EEG: Electroencephalogram

fMRI: Functional magnetic resonance imaging

HPA: Hypothalamic-pituitary-adrenal

HPT: Heat pain threshold

HPTL: Heat pain tolerance level

IASP: International Association for the Study of Pain

IQR: Interquartile range

NRS: Numerical rating scale

OFC: Orbitofrontal cortex

PAG: Periaqueductal grey

PCS: Pain Catastrophising Scale

RM: A collective term which refers to neurons of the pontomedullary raphe magnus and the nucleus reticularis magnocellularis of the rostral ventromedial medulla

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AUTHOR CONTRIBUTIONS

This thesis is a culmination of extensive research and effort conducted primarily by myself, under the expert guidance and supervision of my supervisors, Antonia Wadley and Stella Iacovides, and with the mentorship of Peter Kamerman for my data analysis. The contributions I made to this project are detailed below:

- Survey and Data Capture Design: I was solely responsible for the compilation and implementation of all surveys for both Part 1 and Part 2 of my thesis using RedCap. Customised questionnaires were created by me, incorporating critical input and directions from my supervisors. Additionally, I designed the data capture forms used in Part 2 of my thesis, utilising the RedCap platform.
- Data Collection: I carried out all aspects of data collection. This involved disseminating the online survey from Part 1 across various university platforms and through social media channels. Moreover, I independently executed all Conditioned Pain Modulation data collection procedures, adhering to a protocol that has been previously described in the literature and is detailed in Section 2.3.4.
- Data Analysis: All data analyses were conducted by me, using RStudio. Throughout this process, I was under the guidance of my supervisors and benefitted from the mentorship of Peter Kamerman, which was instrumental in the successful analysis of the data.
- Thesis Writing and Visual Representation: All chapters in this thesis were written by me. Each chapter was subjected to thorough revisions by my supervisors, ensuring the highest academic standards. Furthermore, I personally created all tables and figures presented in this thesis, which serve to visually represent and support the research findings.

These contributions show comprehensive involvement in all stages of the study, reflecting my commitment to the research and the advancement of knowledge in my field of study.

CHAPTER 1

INTRODUCTION

1.1 Overview

Pain is a complex subjective experience with affective and sensory dimensions (Raja et al., 2020). Pain is not simply the result of activity of sensory neurons, but rather, is experienced due to the combined interaction of any combination of nociceptive, affective, cognitive and sensory stimulation (Damien et al., 2018; Raja et al., 2020). In an attempt to encompass the complexity of the pain experience, and in hope that pain management and assessment are improved, the definition of pain has been recently revised by the International Association for the Study of Pain (IASP) (Raja et al., 2020). Pain is now defined as an unpleasant sensory and emotional experience that is always personal and depends on biopsychosocial factors (Raja et al., 2020). Additionally, the updated definition states that the experience of pain can be associated not only with potential or actual damage to tissue, but also with stimuli that *resemble* and *threaten* potential or actual tissue damage (Raja et al., 2020).

Given the highly subjective and personal nature of pain it is not surprising that psychological aspects affecting pain are being increasingly studied. There is growing and compelling evidence that pain is modifiable by various psychological factors including: pain expectation, expectation of pain relief, pain catastrophising, levels of stress, anxiety and depression, distraction from (or attention to) a pain and fear-avoidance behaviours (Colloca and Barsky, 2020; Fields, 2018; Jackson et al., 2012; Karsdorp et al., 2012; Thompson et al., 2016; Timmers et al., 2019; Van Vliet et al., 2021; Vlaeyen et al., 2009). However, research focused on the social aspect of pain is still limited.

The effect of social support on pain perception is the main social factor that has been studied (Edwards et al., 2016). However, the effect of social support on pain interference, dysfunction and pain intensity in individuals with chronic pain is inconsistent, especially between different cultures (Ferreira-Valente et al., 2014). Pain is experienced within a social context and can, therefore, be influenced by the social context (Che et al., 2018; Karos et al., 2018, 2020; Peeters and Vlaeyen, 2011; Vlaeyen et al., 2009). Recent work has suggested a shift to focus on the social aspect of pain and to highlight the importance of studying and treating pain as part of a social context, thus proposing a reappraisal of the biopsychosocial model (Nicholas, 2022).

Taking it one step further, interpersonal relationships are what connect individuals to the social environment and the effect of interpersonal relationships in the context of pain can be studied by using the attachment theory (Meredith et al., 2008; Meredith, 2013), which is essentially a psychobiological system that governs one's behaviours in times of perceived threat (Bowlby, 1969). In the following literature review, I discuss the physiology of pain and the importance of threat, the adult attachment theory, the current evidence between adult attachment and pain (experimental and chronic) and posit that attachment may associate with the development and mechanisms of pain.

First, I will discuss the physiology of pain, highlighting the process of nociception as well as pain modulation. Next, I will break down the relationship between threat and pain perception by looking at both physical and social threats. I will then move on to discuss attachment theory, going into detail on adult attachment. I will explain how adult attachment is classified, how it is activated and what is currently known about its neurobiology. Lastly, I will critically discuss the literature investigating the association between adult attachment and both chronic and experimental pain, highlighting strengths and gaps in previous research. Ultimately, I will state the aims and objectives for my study, which seek to improve the understanding of the association between adult attachment and pain.

1.2 The physiology of pain

Pain is complex and its regulation remains incompletely understood. Details of the complex neurocircuitry have been described (Lee and Neumeister, 2019; Peirs and Seal, 2016), but in brief, peripheral information, which will be described next, is distributed to successions of intricate neural circuits in the dorsal horn of the spinal cord and then to several regions in the brain, generating an array of emotions, actions, and sensations that become the experience of pain (Peirs & Seal, 2016).

Pain can be classified into four broad groups: nociceptive, inflammatory, neuropathic and nociplastic (Fitzcharles et al., 2021; Millan, 2002; Woolf, 2010). Nociceptive pain may occur in the presence of noxious stimuli (such as thermal, mechanical or chemical stimuli) (Woolf, 2010). Nociception is initiated by stimuli that activate the peripheral nociceptors, a highly specialised subset of primary sensory neurons that respond only to high-threshold (and therefore, potentially noxious) thermal, mechanical or chemical stimuli (Sneddon, 2018; Yam et al., 2018). Nociceptors have unmyelinated (C-fibre) or myelinated (Aδ-fibre) axons, which carry the action potentials from the periphery to the central nervous system (Dubin and Patapoutian, 2010; Sneddon, 2018; Yam et al., 2018). Nociception comprises the processes of transduction, conduction, transmission and perception (described in detail in the section 1.2.1 that follows (Dubin and Patapoutian, 2010).

Inflammatory pain usually occurs after damage to bodily tissue (Woolf, 2010). Inflamed/damaged cells release chemicals and recruit various inflammatory markers, including macrophages, mast cells and neutrophils to release more chemicals including prostaglandins and pro-inflammatory cytokines (Chen et al., 2013). These chemicals activate nociceptors and increase their sensitivity to noxious stimuli (causing hyperalgesia) and non-noxious stimuli (making typically non-painful stimuli painful (allodynia)) (Chen et al., 2013). This hypersensitivity to both noxious and non-noxious stimuli serves to discourage movement of the injured area, in order to facilitate the healing process and minimise further damage (Chen et al., 2013; Woolf, 2010). Nociceptive pain and inflammatory pain are mostly "adaptive" forms of pain in that they contribute to the survival of an organism from injury, either in the form of an early warning signal of a threat (nociceptive pain), or by reducing movement and allowing for cellular repair in already-damaged tissue (inflammatory pain) (Woolf, 2010).

Nociceptive and inflammatory pain are also typically acute in nature. However, nociceptive and inflammatory pain can become chronic when pain persists, even after the wound has healed in some cases (Treede et al., 2019; Woolf, 2010). Chronic pain can also exist without the presence of tissue damage due to central sensitisation (Treede et al., 2019; Woolf, 2010). Central sensitisation refers to an amplification of neural signaling within the central nervous system, leading to pain hypersensitivity even in the absence of peripheral noxious stimuli. This phenomenon can increase the degree, duration, and spatial extent of pain, uncoupling it from specific external stimuli (Woolf, 2011). Chronic pain is defined as pain that persists for longer than three months (Treede et al., 2019), and is considered as pathological, maladaptive pain as it has no biological advantage (Woolf, 2010). Pathological pain can occur after damage to the nervous system (neuropathic pain) following, for example, trauma (e.g. spinal cord injury), metabolic diseases (e.g. diabetes), viral infections (e.g. HIV), or cancer (Colloca et al., 2017; Kuner, 2010; Verma et al., 2005). In addition, pathological pain can occur when no tissue damage or inflammation has occurred (nociplastic pain), as is the case in central sensitisation syndromes such as fibromyalgia and irritable bowel syndrome (Fitzcharles et al., 2021). In brief, the transition from acute to chronic pain involves mechanisms of peripheral and central sensitisation (Pak et al., 2018; Voscopoulos and Lema, 2010) as well as dysfunction in the descending modulation of pain due to plasticity in the rostral ventromedial medulla (Chen and Heinricher, 2019). In peripheral sensitisation, repeated stimulation lowers the activation threshold of nociceptors due to the release of inflammatory molecules, leading to an increased sensitivity to pain (hyperalgesia) (Pak et al., 2018; Voscopoulos and Lema, 2010). Molecular changes (such as upregulated excitatory receptors and altered ion channel expression) and neuroplastic changes (such as the remodeling of neuronal synapses by glial cells) further increase the sensitivity to pain by amplifying the response to the noxious stimulus (Pak et al., 2018; Voscopoulos and Lema, 2010). Central sensitisation further acts in increase pain sensitivity with persistent pain signals enhancing the sensitivity of the central nervous system (Pak et al., 2018). Neurotransmitters like substance P and glutamate reduce activation thresholds in spinal neurons, while diminished inhibitory control and upregulation of NMDA receptors result in the perception of low-level stimuli as intense pain (Pak et al., 2018). This process, coupled with structural changes in neuronal pathways, results in allodynia, marking the complex transition from acute to chronic pain (Pak et al., 2018). For the purpose of this literature review, however, I will now focus specifically on nociceptive pain.

1.2.1 The process of nociception and modulation of pain

Impulses from nociceptors travel along Aδ and C fibres, which project into the dorsal horns of the spinal cord and ascend to supraspinal regions via the spinothalamocortical pathways located in the white matter region of the spinal cord (Rainville, 2002; Yam et al., 2018). Other projection neurons transmit nociceptive impulses to the brain via the parabrachial nucleus and the amygdala, contributing to the experience of pain (Yam et al., 2018). Neural imaging studies have identified the areas of the brain that are activated by nociceptive stimuli, including the periaqueductal grey (PAG) region of the midbrain, rostral anterior cingulate cortex, amygdala and the somatosensory cortices (primary and secondary) (Ossipov et al., 2010). These brain areas are involved in the interpretation of nociceptive stimuli intensity and location and they act to modulate these stimuli, giving rise to the experience of pain (Ossipov et al., 2010; Yam et al., 2018).

The perception of pain may result from ascending transmission of nociception to supraspinal regions but can also be modulated via descending pain pathways. Neurons in the PAG in the midbrain integrate ascending and descending information (Yam et al., 2018). The PAG neurons then stimulate the ‘RM’, a collective term which refers to neurons of the pontomedullary raphe magnus and the nucleus reticularis magnocellularis of the rostral ventromedial medulla (Mason, 1999; Ossipov et al., 2010; Yam et al., 2018). The RM neurons project into the dorsal horn of the spinal cord and have been found to either augment or reduce neuronal activity from nociceptive stimuli and influence pain, both directly and indirectly (Ossipov et al., 2010).

The type of RM neurons stimulated by the PAG neurons (and thus whether activity from nociceptive stimuli is facilitated or inhibited) depends on the supraspinal processing of the noxious stimuli and its integration in the PAG (Mason, 1999; Yam et al., 2018). When the “on” RM neurons are activated following noxious stimuli, they are proposed to mediate noxious facilitation. Conversely, when the “off” RM neurons are activated following noxious stimuli, they have been proposed to mediate noxious stimuli inhibition (Mason, 1999). The “on” and “off” neurons may, therefore, be involved in the noradrenergic and serotonergic pathways that form part of descending brainstem pain modulation (Figure 1.1). Noradrenaline and serotonin are the key neurotransmitters in the descending modulation of pain, both may facilitate or inhibit the perception of pain, depending on which receptors are activated (Iacovides et al., 2021). The pathway of nociceptive impulses from the brain to RM neurons via PAG neurons illustrates the modulation of pain through descending pathways (Ossipov et al., 2010; Yam et al., 2018) (Figure 1.1).

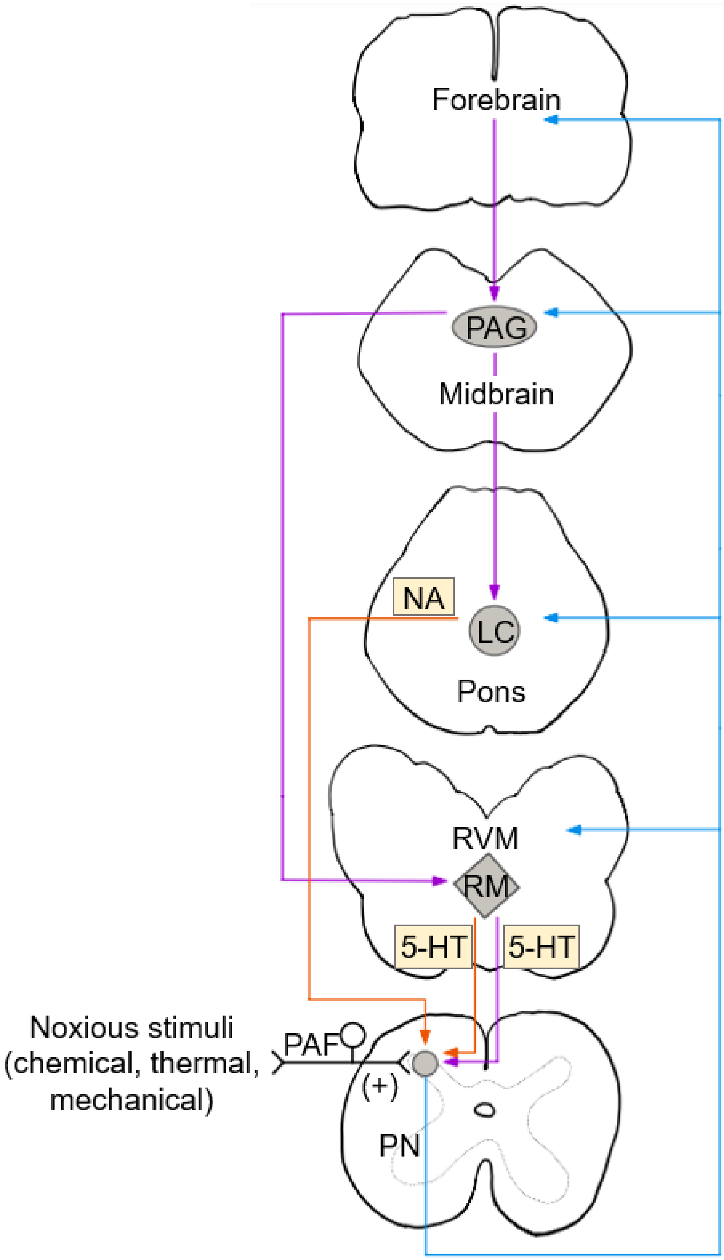

Figure 1.1: The ascending transmission and descending modulation of a noxious stimulus. *A noxious stimulus stimulates the projections neurons (PN) in the dorsal horn of the spinal cord via primary afferent fibres (PAF), initiating the ascending transmission (blue arrows) of the stimulus. The PN project to the nucleus raphe magnus (RM), pontine locus coeruleus (LC) and periaqueductal grey matter (PAG) via the spinobulbar tract and onwards to the limbic forebrain via the spinothalamic tract. For the descending modulation (purple arrows for facilitatory modulation, orange arrows for inhibitory modulation), the limbic forebrain has outputs to the PAG in the midbrain, which in turn, projects to the LC in the rostral pons and the RM in the rostral ventromedial medulla (RVM). The LC gives rise to noradrenergic (NA) projections to the dorsal horn, which inhibit (orange arrow) the transmission of afferent nociceptive information through the dorsal horn. The RVM gives rise to serotonergic (5-HT)*

projections to the dorsal horn that can either facilitate (purple arrow) or inhibit (orange arrow) transmission of nociceptive information (Iacovides et al., 2021).

1.2.2 Mechanisms of Conditioned Pain Modulation

There are many inhibitory circuits for nociceptive stimuli but one in particular, conditioned pain modulation (CPM), can be measured in the laboratory using quantitative sensory tests (Damien et al., 2018; Nir and Yarnitsky, 2015). Protocols testing CPM are therefore measuring endogenous analgesia (Damien et al., 2018; Nir and Yarnitsky, 2015). CPM was first studied in rats where it was referred to as the diffuse noxious inhibitory control (DNIC) pathway (Le Bars et al., 1979). It has been suggested, however, that DNIC is more complex than simply the inhibition of the neurons in the dorsal horn (Le Bars et al., 1979; Nir and Yarnitsky, 2015; Yarnitsky et al., 2010). The term CPM effect was, therefore, adopted to describe the phenomenon when the perception of pain from one nociceptive stimulus is decreased by a second simultaneous nociceptive stimulus, as measured by a test paradigm (Nir and Yarnitsky, 2015; Yarnitsky, 2010; Yarnitsky et al., 2010). As such, the CPM effect provides a measure of endogenous analgesia (Nir and Yarnitsky, 2015).

While the underlying mechanisms of CPM are not fully understood, supraspinal and cerebrospinal mechanisms appear to play a role in how CPM affects endogenous analgesia (Damien et al., 2018). Indeed, a recent study found that an efficient CPM effect was associated with an increased functional connectivity between the PAG and brain regions that are associated with the modulation of pain (the motor and premotor cortices, somatosensory cortices and the dorsolateral prefrontal cortex) (Harrison et al., 2022). Moreover, the inhibitory CPM effect has been found to coincide with reductions in the blood-oxygen-level-dependent responses in the primary and secondary somatosensory, dorsolateral prefrontal and premotor cortices, further shedding light on the possible mechanisms underlying the CPM effect (Harrison et al., 2022). CPM occurs when a noxious stimulus recruits enough peripheral nerves and stimulates enough “off” neurons to inhibit another noxious stimulus by suppressing neuronal responses in the dorsal horn of the spinal cord (Kennedy et al., 2016; Le Bars et al., 1979; Mason, 1999; Nir and Yarnitsky, 2015; Ossipov et al., 2010). Essentially in CPM, the convergent neurons in the dorsal horn get excited by a noxious stimulus which then ascends to supraspinal regions, triggering DNIC (Le Bars et al., 1979). Through DNIC, further excitation of convergent neurons that are not already excited is inhibited, resulting in reduced pain of a second noxious stimulus (Le Bars et al., 1979) (Figure 1.2). Still the mechanisms underlying the CPM effect are not well understood since the application of an event-related design to investigate CPM presents significant challenges (Harrison et al., 2022). Firstly, the equipment conventionally employed for CPM assessment, such as water baths, thermal stimulators, and metallic algometers, exhibit limitations in the context of a neuroimaging environment (Harrison et al., 2022). Secondly, the co-presentation of test and conditioning stimuli complicates the isolation of the specific effects of modulation on pain perception (Harrison et al., 2022).

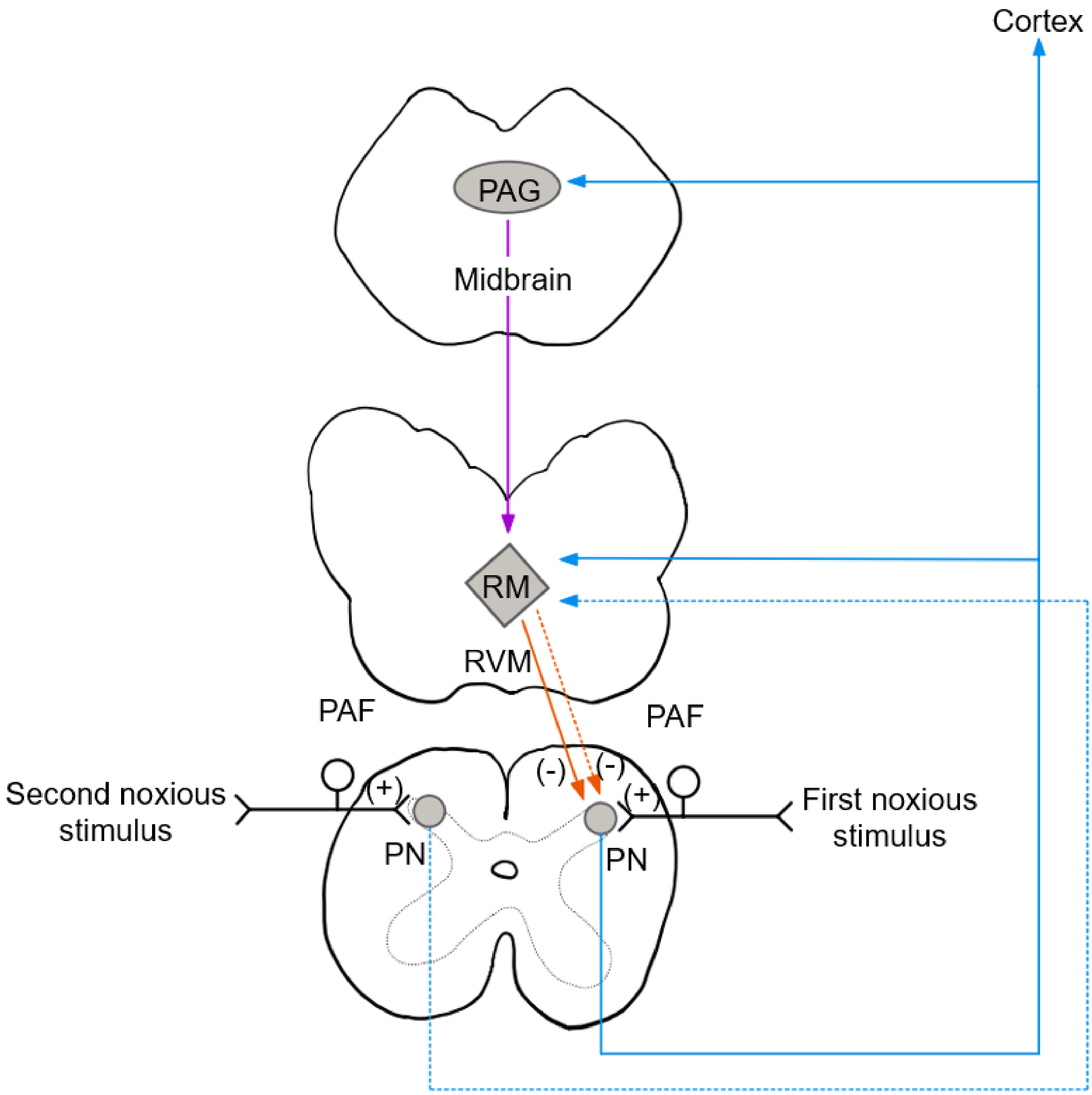

Figure 1.2: The process of conditioned pain modulation. *The first noxious stimulus (pathway indicated by a solid arrow) stimulates convergent neurons in the dorsal horn of the spinal cord which, in turn, stimulates projection neurons (PN). The PN transmits the stimulus to the cortex and the periaqueductal grey matter (PAG) in the midbrain. Neurons in the PAG stimulate neurons in the nucleus raphe magnus (RM) located in the rostral ventromedial medulla (RVM), which then inhibit (solid orange arrow) further stimulation of convergent neurons in the dorsal horn. A second noxious stimulus (pathway indicated by a dotted arrow) stimulates PN to transmit the stimulus to the RM, but further stimulation of the convergent neurons is inhibited (orange dotted arrow) by neurons in the RM. PAF: primary afferent fibre* (Le Bars et al., 1979; Nishino, 2011). *Blue arrows represent ascending pathways, purple arrows represent descending facilitatory pathways and orange arrows represent descending inhibitory pathways.*

When determining the CPM effect using the CPM test paradigm, the first noxious stimulus is the one that the CPM effect will be measured on and is termed the "test stimulus" (Yarnitsky et al., 2010). The second noxious stimulus is used to induce a change in pain perception, thereby inducing the CPM effect, and is termed the "conditioning stimulus" (Yarnitsky et al., 2010). The test stimulus is applied to a part of the body, usually a part of a limb, and the perception of the pain caused by the test stimulus is measured, most often, by subjective pain ratings (Damien et al., 2018; Ibancos-Losada et al., 2020; Yarnitsky et al., 2010). Thereafter, the conditioning stimulus is applied to a separate, contralateral part of the body, which theoretically reduces the pain intensity of the test stimulus if the conditioning stimulus is painful enough (Ibancos-Losada et al., 2020; Klyne et al., 2015); a score greater than 20 on a 100-point numerical pain scale, indicating mild-to-moderate pain levels, is typically enough to induce a modulatory effect (Granot et al., 2008; Nir et al., 2011; Willer et al., 1984).

The CPM test paradigm, therefore, assesses DNIC which is said to be a dynamic pain measure as it represents the dynamic endogenous modulatory processes of pain (Nir et al., 2011). Static pain measures, such as pain threshold and pain tolerance, reflect pain intensity but do not measure any underlying mechanism of pain modulation (Nir et al., 2011).

1.2.3 Physiological and psychological influences on conditioned pain modulation

There is evidence that the CPM effect involves the interaction between both physiological *and* psychological processes (Bjørkedal and Flaten, 2012; Nir and Yarnitsky, 2015; Yarnitsky, 2010). CPM is influenced by behavioral responses to pain and has been found to be affected by cognitive factors such as expectation, pain catastrophising, psychological stress and anxiety (Bjørkedal and Flaten, 2012; Nir and Yarnitsky, 2015). Neurotransmitters (serotonin, noradrenalin and dopamine) involved in the physiology of pain and in psychological factors associated with pain, are suggested to link the psychological and physiological aspects of CPM (Nir and Yarnitsky, 2015). These neurotransmitters are also reported to contribute to varying personality trait expression, such as engaging in harm avoidance or novelty seeking behaviours, suggesting a possible interaction between physiological and psychological pathways involved in pain (Nir and Yarnitsky, 2015).

Similar brain regions have also been found to be involved in both the physiological and psychological aspects of pain (Moont et al., 2010). Specifically, the insula and anterior cingulate cortex (ACC) play a role in the motivational-affective component of pain during distraction, and have also been found to be involved in CPM (Moont et al., 2010). Both distraction (psychological) and CPM (physiological) interventions significantly decreased the test stimulus pain unpleasantness and intensity when tested separately. Moreover, when distraction was tested together with CPM, there was an additive pain inhibitory effect (Moont et al., 2010). It is, therefore, suggested that the analgesic effects of CPM and distraction act independently, and so their respective pathways may originate from different regions within the insula and ACC (Moont et al., 2010).

Moreover, studies using the CPM test paradigm have also demonstrated how pain modulation is affected by pain catastrophising, (Bjørkedal and Flaten, 2012; Nir and Yarnitsky, 2015) and expectations (Bjørkedal and Flaten, 2012; Damien et al., 2018; Nir et al., 2012). A study conducted on 48 healthy male participants found that when the participants expected the conditioning stimulus to be less painful than when they experienced it for the first time, the CPM effect was reduced. Thus, participants produced lower endogenous analgesia in response to the conditioning stimulus, despite the stimulus being of the same intensity as the first exposure (Nir et al., 2012). In another study of 72 healthy participants, when participants expected the conditioning stimulus to *increase* the pain of the test stimulus (rather than the normal CPM response, which is to decrease pain), the CPM effect (pain inhibition) was reduced (Bjørkedal and Flaten, 2012). Collectively, these studies demonstrate how learned responses (placebo and nocebo conditioning) alter the expectation, and consequently, alter pain perception by influencing the direction and extent of the CPM effect (Bjørkedal and Flaten, 2012; Damien et al., 2018; Nir et al., 2012).

The CPM test paradigm has also been used to assess endogenous analgesia in individuals living with chronic pain (Damien et al., 2018; Nir and Yarnitsky, 2015; D. Yarnitsky et al., 2015). CPM is reported to be impaired (little or no CPM analgesia occurs) in individuals with chronic pain and idiopathic pain syndromes, (Damien et al., 2018; Nir and Yarnitsky, 2015; Ossipov et al., 2010). Impaired CPM is possibly due to compromised neural mechanisms (as a result of the chronic pain) that convey endogenous analgesia (Nir and Yarnitsky, 2015), or CPM efficacy may predict the likelihood of developing chronic pain (Damien et al., 2018; Yarnitsky et al., 2008). Either way, better functioning of the CPM inhibitory pathway has been found to be associated with less chronic pain and better quality of life (Damien et al., 2018).

1.3 Threat and pain perception

1.3.1 Physical threat and pain

Our nervous systems are primed to detect if we are safe or in danger (Donnelly et al., 2020). As mentioned above, pain may be adaptive in that it serves to alert and protect us from potentially harmful stimuli, motivating us to take action (promote survival) when there is harm or a threat of harm to our bodies (Donnelly et al., 2020). Additionally, it has been shown that individuals report increased pain intensities when they perceive their environment (social threat) or the painful stimulus (physical threat) as more threatening (Leung, 2012; Peeters and Vlaeyen, 2011; Timmers et al., 2019; Todd et al., 2016; Wang et al., 2016). As such, pain perceptions are affected by threat appraisals of painful stimuli, which may be influenced by social contexts (Boston and Sharpe, 2005; Todd et al., 2016; Van Vliet et al., 2021; Vlaeyen et al., 2009).

There have been well-powered studies in healthy individuals investigating the effect of the perception of physical threat of a stimulus on pain reporting by manipulating threat appraisals of the cold pressor test stimulus prior to the experiment (Boston and Sharpe, 2005; Todd et al., 2016). The healthy participants in these studies were randomly divided into two groups: threat and no-threat/neutral (Boston and Sharpe, 2005; Todd et al., 2016; Vlaeyen et al., 2009). The participants in the threat group were manipulated into perceiving the cold pressor test stimulus as more threatening than it was by changing the name and description of the procedure (Boston and Sharpe, 2005; Todd et al., 2016). More specifically, the procedure was called a ‘vasodilation task’ and was described using medical terminology, making the procedure seem more physically threatening (Boston and Sharpe, 2005; Todd et al., 2016). Other studies manipulated the physical threat perception by leading participants to believe that normal signs from the cold pressor test were harmful and indicative of frost bite (Vlaeyen et al., 2009; Wang et al., 2016). Both these studies, plus others, show that participants in the threat groups report increased pain intensity and decreased pain tolerance compared to the no-threat (control) groups (Boston and Sharpe, 2005; Todd et al., 2016; Vlaeyen et al., 2009; Wang et al., 2016).

The perception of physical threat also impacts the efficacy of pain coping strategies (Jackson et al., 2012; Wang et al., 2016). In healthy participants, pain coping strategies, such as distraction and acceptance, have been shown to effectively reduce experimental cold pain when a stimulus is perceived as low threat (the benign nature of the cold pain) (Jackson et al., 2012; Wang et al., 2016). However, when noxious stimuli are perceived as highly threatening (likely to induce frost bite, for example), distraction and acceptance are reported to no longer be effective pain coping strategies (Jackson et al., 2012; Wang et al., 2016). Furthermore, in chronic pain, it has been suggested that distraction and acceptance may not be effective strategies to reduce pain, especially when the pain is believed to be causing physical harm (Jackson et al., 2012). It may be more beneficial, therefore, to reduce the perception of threat as part of pain coping strategies in both chronic and acute pain (Wang et al., 2016).

1.3.2 Social threat and pain

The link between social context and pain has been demonstrated in various studies by looking at social threat (Karos et al., 2018, 2020; Peeters and Vlaeyen, 2011) and social support (Che et al., 2018; Vlaeyen et al., 2009). Similarly to perception of physical threat mentioned in Section 1.3.1 above, It has been found that individuals who perceive a social context as highly threatening, also perceive the painful stimulus as more threatening and have increased pain perceptions compared to individuals who do not view a situation as threatening (Karos et al., 2018, 2020). This relationship was demonstrated in a study through manipulating the social threat by pseudo-participants seemingly delivering more (high threat) or less (low threat) noxious stimuli to the real participant than what the experimenter allowed. Yet, each group received the same number of noxious stimuli at the same intensity (Karos et al., 2020). More specifically, participants in both groups received 10 noxious electrocutaneous stimuli that were administered by a seemingly uninvolved confederate. The pseudo-participant in the high-threat group was informed, in front of the participant, that they could "choose" from 1-10 the number of stimuli of a set intensity to administer to the participant. The pseudo-participant in the low-threat groups, however, was told to "choose" from 10-20 stimuli to administer to the participant. The pseudo-participant in the high-threat group seemingly chose the most number of stimuli (10 in a range of 1-10), appearing more threatening to the participants compared to the confederates in the low-threat group, who seemingly chose the least number of stimuli (10 in a range of 10-20) (Karos et al., 2020). Ultimately, participants in the high-threat group reported higher pain intensity and unpleasantness compared to the participants in the low-threat group (Karos et al., 2020).

1.3.3 Pain, threat and stress

A theoretical model proposed by Timmers *et al.* (2019) links chronic pain with stress through a process called "threat learning". Threat learning is suggested to be the body's response to a threat that enables it to learn from the threatening experience and adapt the body's behaviour to that threat in the future (Timmers et al., 2019). Threat-learning may, therefore, be described as a process resulting in a negative expectation of pain brought about by previous physical (adverse effects from medication) or social (observation of pain in somebody else) experiences (Colloca and Barsky, 2020). Pain-related threat is believed to facilitate activation of the hypothalamic-pituitary-adrenal (HPA) axis stress response (Timmers et al., 2019). Indeed, this suggestion is in line with current nocebo literature showing that the negative expectation of experimental pain (brought about by the nocebo effect) may be associated with the activation of the HPA axis (Colloca and Barsky, 2020). The HPA axis' response to a more physically threatening stimulus is proposed to amplify the nociceptive pathways of the stimulus, resulting in increased pain perceptions (Timmers et al., 2019).

Furthermore, the relationship between stress and threat is believed to be bidirectional (Timmers et al., 2019). Acute stress has been found to enhance amygdala and salience network interactions, resulting in increased threat processing and an increase in attention to threat (Timmers et al., 2019). It has, therefore, been suggested that acute stress causes an attentional bias towards threatening information, resulting in potentially harmful stimuli being perceived as more physically threatening compared to stimuli in the absence of stress (Timmers et al., 2019). By stress increasing the perceived threat of a painful stimulus, stress is likely to elicit immediate pain control behaviours, such as pain avoidance strategies (Timmers et al., 2019). Thereafter, stress also appears to create a bias memory towards new threat information over other information. As such, threat memories will be created first when under stress (Giustino and Maren, 2018; Timmers et al., 2019). Acute stress may also reduce the ability to retrieve memory information that is unrelated to threat, therefore, threat memories are also retrieved first over other information (Timmers et al., 2019).

In essence, the perception of physical (harmful or adverse effects) or social (negative patient-provider interactions) threat may lead to a negative evaluation of pain with expectations of increased pain intensity, leading to increased reporting of pain intensity (Colloca and Barsky, 2020; Weimer et al., 2020). Likewise, when threat (physical or social) is perceived as low, there may be an expectation of less severe pain, resulting in a deceased perception of pain intensity (Colloca and Barsky, 2020; Weimer et al., 2020). Importantly, the evaluation of a threat does not only happen in the moment, but rather is shaped by memories of previous experiences, including childhood experiences (Bowlby, 1969; Mikulincer and Shaver, 2007). One way to understand and measure how individuals might evaluate threats may be to explore adult attachment.

1.4 Attachment theory

It has been proposed that the origins of certain coping strategies, pain behaviours and pain perceptions may be rooted in adult attachment style, which stems from the "Attachment Theory" (Meredith et al., 2008). Attachment theory suggests that humans possess an innate psychobiological system (the attachment system) that has developed through evolution to ensure the survival of infants (Bowlby, 1969). The attachment system in infants is proposed to develop in response to early interactions and relationships between the infant and primary caregiver (Bowlby, 1969). This system is primarily activated when the infant feels threatened (physically or emotionally) and it governs the presentation of attachment behaviours in infants

(Bowlby, 1969, 1973). Attachment behaviours, such as smiling or crying, serve to encourage proximity and attention from the infant's caregiver as a way of ensuring support and protection from the perceived danger (Bowlby, 1969, 1973). The level of activation of the attachment system depends on an infant's attachment style (based on early interactions and described in detail below), and determines which attachment behaviours are used in the presence of threat (Ainsworth and Bell, 1970; Bowlby, 1969).

The attachment system is suggested to play a role throughout life, giving rise to the adult attachment theory (Bartholomew and Horowitz, 1991). Adult attachment theory reflects how individuals perceive themselves and others, as determined by early relationships with the primary caregiver (Bartholomew and Horowitz, 1991; Mikulincer and Shaver, 2007). These factors provide a framework for how individuals behave and what they will expect from interpersonal relationships in adulthood, particularly in situations that are perceived as threatening (Bartholomew and Horowitz, 1991; Kowal et al., 2015; Meredith et al., 2008; Mikulincer and Shaver, 2007). Similar to infant attachment, the level of activation of the adult attachment system is dependent on the individual's adult attachment style, which governs their adult attachment behaviours in response to a perceived threat (Bowlby, 1969; Mikulincer and Shaver, 2007). Adult attachment behaviours are presented as a means of eliminating the threat and maintaining a safe equilibrium in interpersonal relationships.

Attachment theory originally described various "attachment styles" to categorise the attachment behaviours of infants, based on the principal that infants develop specific attachment behaviours depending on the relationship they have with their caregiver (Ainsworth and Bell, 1970; Bowlby, 1969). The attachment theory was derived by analysing infant behaviour with their primary caregiver by using the "strange situation" test (Ainsworth and Bell, 1970; Bowlby, 1969). In the strange situation test, infant's behaviours in the a) presence, b) absence, and c) return of their mothers, defines their attachment styles (described in detail below) (Ainsworth and Bell, 1970; Bowlby, 1969). Infants were later found to develop those same attachment behaviours to any primary caregiver (not only with mothers) (Bowlby, 1973). The individuals at which the attachment behaviours are most often directed, have been termed "attachment figures" (Bowlby, 1969).

An infant's attachment style, which governs their attachment behaviours, is rooted in how dependent they are on their attachment figure as a source of security (Ainsworth and Bell, 1970). From the "strange situation" experiment, three attachment styles were proposed and they describe how the infants react to the absence and return of their attachment figure (Ainsworth and Bell, 1970; Ainsworth, 1979). The first infant attachment style is the "Secure attachment", describing infants as distressed when their caregiver leaves but are quickly reconciled upon their return (normal activation of attachment system) (Ainsworth, 1979). The second attachment style is the "anxious-ambivalent attachment", which describes infants as intensely distressed by separation from their caregiver, yet show ambivalent behaviour (both seeking and resisting contact) upon their caregiver's return (hyper-activation of attachment system) (Ainsworth, 1979). The third attachment style is the "avoidant attachment", where the infant shows almost no signs of distress upon separation from, and avoids contact with, their caregiver/attachment figure upon their return (hypo-activation of attachment system) (Ainsworth, 1979).

Initially, attachment behaviours in infants are reported to consist of fixed patterns, such as smiling and crying to attract attention, or an attempt to maintain contact through grasping and sucking (Ainsworth, 1979). These fixed-pattern behaviours are not directed at a specific figure or with a specific goal in mind, but are rather used as general signaling to attract caregivers' attention (Ainsworth, 1979). As the infant grows and is able to distinguish different caregivers from one another, the attachment behaviours become more organised and goal-driven, such as crying, screaming or smiling to elicit a specific response from the caregiver (not simply general proximity) (Ainsworth, 1979). In other words, the infants will persist with various behaviours, or alter their behaviours, based on feedback from their caregiver, until their attachment goal is reached (e.g. physical touch from attachment figure) (Ainsworth, 1979).

The attachment style of an infant is believed to develop within the first year of life and to become progressively more stable with increasing age (Ainsworth, 1979; Bowlby, 1969). Importantly, attachment styles formed as infants are believed to influence social relationships later in life, forming adult attachment styles (Hazan and Shaver, 1987; Kahn and Antonucci, 1980). Although adult attachment styles and subsequent behaviours are rooted in early relationships between infant and caregiver and are believed to be relatively stable throughout adulthood (Bartholomew and Horowitz, 1991; Chopik et al., 2019; Mikulincer and Shaver, 2007), they can also change over time depending on the level of childhood trauma, the security of new relationships (such as with a best friend or romantic partner), or due to attachments formed with new-born children (Chopik et al., 2019; Doherty and Feeney, 2004; Yumbul et al., 2010).

1.5 Overview of adult attachment

As with the infant attachment system, the extent to which the adult attachment system is activated during times of stress is dependent on one's adult attachment style, influencing interpersonal relationships in adulthood (Bartholomew and Horowitz, 1991; Bowlby, 1969; Mikulincer and Shaver, 2007; Sable, 2008). Furthermore, it has been noted that although attachment in adulthood is not as obvious as childhood attachment, it is still present and is believed to be important for understanding adult interpersonal relationships (Hazan and Shaver, 1987; Kahn and Antonucci, 1980; Sable, 2008). Individuals within a person's closest social circle have been suggested to act as attachment figures (Kahn and Antonucci, 1980). As such, these are the individuals that one would turn to in times of need, and they have been suggested to be essential for one's general wellbeing throughout life (Kahn and Antonucci, 1980; Sable, 2008).

Importantly, the expansion of adult attachment theory and the classification of adult attachment into specific adult attachment styles was initially based on assessment of romantic attachments (Hazan and Shaver, 1987). Three adult attachment styles (Secure, Anxious-ambivalent, and Avoidant) that appeared to persist from childhood have been proposed (Hazan and Shaver, 1987). These adult attachment styles were proposed to govern an individual's beliefs about relationships, beliefs about other people, and their own self-worth (Hazan and Shaver, 1987). Essentially, adults with "Secure attachment" have a strong belief in themselves and in others, meaning that they believe that they are worthy of love and support, and they believe that their attachment figures will provide love and support when they ask for it. Adults with poor self-belief (believe they unworthy of love and support) are described to have an “anxious-ambivalent attachment style”, and those with a poor belief in others (believe love and support is unavailable to them) are classified as having an “avoidant attachment style” (Bartholomew and Horowitz, 1991; Hazan and Shaver, 1987). In this model, the “avoidant adult attachment style” described individuals that were emotionally detached and did not seek comfort from their romantic partners in times of need (Hazan and Shaver, 1987).

A concern about the three-category model, however, was that some individuals classified as “avoidant” also showed signs of anxiety over whether their partner would provide them with support, should they need it (Bartholomew, 1990; Mikulincer and Shaver, 2007). As such, some individuals displayed signs of both avoidance and anxiety, and hence should not simply fall into the “avoidant” attachment style (Bartholomew, 1990; Mikulincer and Shaver, 2007). The three-category model of adult attachment does not, therefore, encompass a style that describes both a poor belief in oneself as well as others (Bartholomew and Horowitz, 1991). To account for this overlap, a new model was proposed to encompass four categories of adult attachment that occur as a result of the perception of self and the perception of others (Bartholomew and Horowitz, 1991). The four-category model has since been widely used in the attachment literature and will, therefore, be used as the model for adult attachment in this review (Bookwala and Zdaniuk, 1998; Fraley et al., 2000; Guerrero, 1996; Kowal et al., 2015; Meredith et al., 2008).

1.5.1 The four-category model of attachment

The four adult attachment styles are also suggested to stem from infant attachment styles (Bartholomew, 1990; Bartholomew and Horowitz, 1991). Furthermore, emphasis was placed on two dimensions that were found to underlie these four adult attachment styles: 1) anxiety/distress over abandonment and 2) avoidance of intimacy (Bartholomew, 1990; Bartholomew and Horowitz, 1991; Mikulincer and Shaver, 2007). Greater attachment anxiety is synonymous with a worse perception of oneself. In other words, individuals who have poor self-belief constantly seek love and support from others but they do not believe that they are worthy of it, resulting in them becoming anxious (Bartholomew, 1990; Bartholomew and Horowitz, 1991). Greater avoidance is synonymous with a worse perception of others, meaning that a person will avoid others and interpersonal interaction because they are distrustful of others (Bartholomew, 1990; Bartholomew and Horowitz, 1991).

The dimensions of perception of self and others have been arranged to represent four quadrants created by degrees of belief in self versus belief in others (Figure 1.3) (Bartholomew, 1990; Bartholomew and Horowitz, 1991). In attachment literature, the belief in self is referred to as the anxiety over attachment dimension (attachment anxiety), while the belief in others is referred to as the avoidance of intimacy dimension (attachment avoidance) (Bartholomew and Horowitz, 1991). To account for all possible pairings of the models of self and others, the quadrant classification proposed the following four categories: “Secure”, “Dismissing”, “Preoccupied” and “Fearful”. The “Preoccupied” adult attachment style is synonymous with the “Anxious-ambivalent” of the three-category attachment style, while “Dismissing” and “Fearful” attachment styles both stem from the ”Avoidant” three-category attachment style (Bartholomew, 1990). The Dismissing, Preoccupied and Fearful attachment have been collectively described as “Insecure attachment” and involve low belief in self (high attachment anxiety) and/or low belief in others (high attachment avoidance) (Figure 1.3) (Bartholomew and Horowitz, 1991; Mikulincer and Shaver, 2007).

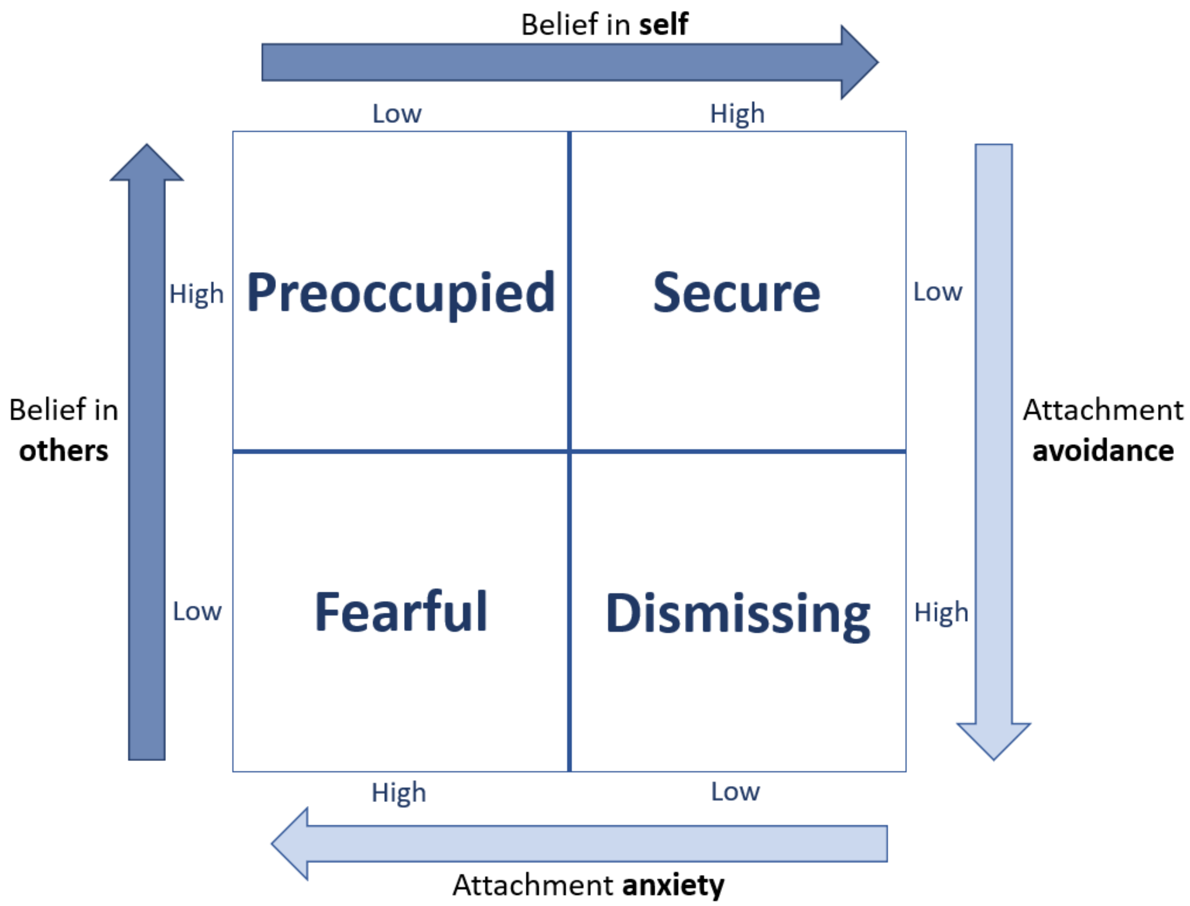

Figure 1.3: The four adult attachment styles based on the model of adult attachment described in Bartholomew and Horowitz (1991).

It is important to note that while the four-category model is widely used and accepted in literature, the results are seldom reported for each category. The majority of authors that have used four adult attachment styles in their research, have chosen to analyse and report their data in terms of the attachment anxiety and avoidance dimensions (Anders and Tucker, 2000; Ein-Dor et al., 2011; Read et al., 2018; Vrtička, Sander, et al., 2012). Consequently, there is a dearth of specific data reported about each attachment style, which are created through the intersection of the attachment dimensions. Many of the studies reviewed here will, therefore, be discussed in terms of levels of attachment anxiety and avoidance, rather than the four specific attachment categories.

1.5.2 Adult attachment behaviours occur when under threat

The degree to which the adult attachment system is activated is determined by the level of perceived threat and, thus, the presentation of attachment behaviours, is dependent on an individual's adult attachment style (Bowlby, 1969; Mikulincer and Shaver, 2007). An individual's adult attachment style influences their perception of threat, and it is this subjective threat appraisal that affects the activation of the attachment system (Long et al., 2020; Mikulincer and Shaver, 2007). When securely attached individuals (high belief in self and others) perceive a threat, their threat appraisal is measured and occurs after careful evaluation of the environment and potential threat (Ein-Dor, 2014). This measured threat appraisal is proposed to be accompanied by positive memories and thoughts about support from attachment figures (Mikulincer and Shaver, 2007). This positive association with attachment figures results in presentation of attachment behaviours such as seeking support and proximity from attachment figures during threatening situations (Long et al., 2020; Mikulincer and Shaver, 2007). Conversely, when insecurely attached individuals (low belief in self and/or others) perceive a threat, their threat appraisal has been shown to be accompanied by negative thoughts and memories about their attachment figures, which is suggested to result in either constant seek of support by others, or avoidance of intimacy with others (Long et al., 2020; Mikulincer and Shaver, 2007).

Individuals who have high attachment anxiety (preoccupied adult attachment style) have been suggested to view their attachment figures as unreliable in times of need, yet these individuals still crave their support since they do not believe they can cope on their own (poor sense of self) (Bartholomew and Horowitz, 1991; Mikulincer and Shaver, 2007). As a result, anxiously attached individuals have shown to be continuously hypersensitive to detecting threat and continuously monitor their surrounding for threats, being very quick to identify a perceived threat (Ein-Dor, 2014; Long et al., 2020; Mikulincer and Shaver, 2007). This swift threat perception results in an overreaction of emotions and constant seeking of support and affirmation from their attachment figures (Ein-Dor, 2014; Long et al., 2020; Mikulincer and Shaver, 2007). Individuals who have high attachment avoidance (dismissive adult attachment style) have been shown to downgrade their threat appraisals, thus being less vigilant to potential threats and are more delayed in their threat perceptions (Ein-Dor, 2014; Ein-Dor et al., 2011). Avoidant individuals are suggested to view their attachment figures as unreliable, but these individuals have a positive sense of self (Bartholomew and Horowitz, 1991; Mikulincer and Shaver, 2007). As such, when these individuals do appraise a situation as threatening, they display little or no attachment behaviours;

they withdraw and do not seek proximity to others as they are said to "downplay" the level of threat (Long et al., 2020; Mikulincer and Shaver, 2007). Lastly, although the sensitivity to detecting a threat for individuals who have both high attachment anxiety and avoidance (fearful adult attachment style) is not directly discussed in the literature, their threat appraisal patterns are possibly a combination of hyper- and hypo-vigilance to danger, depending on the situation. Such an assumption can be drawn due to evidence suggesting that when fearfully attached individuals perceive a threat, they display ambivalent behaviour where they alternate between seeking and withdrawing from support and proximity to others (Mikulincer and Shaver, 2007).

1.5.3 The neurophysiology of the adult attachment system

Although the literature is in its infancy, there is evidence of neurophysiological mechanisms underlying attachment theory, where exposure to a threat results in activation of brain regions responsible for social withdrawal and/or social engagement (Long et al., 2020; Vrtička et al., 2008; Vrtička and Vuilleumier, 2012). A model the neurophysiological systems activated by individual adult attachment styles has been proposed, based on the combined results of multiple studies on the neuroscience of attachment using cohorts of adults, adolescents, children, clinical and non-clinical samples (Long et al., 2020). This model, however, does not include the fearful adult attachment style (Long et al., 2020).

Based on neuroimaging evidence, it has been proposed that the adult attachment system is organised into an affective/emotional system and a cognitive system (Long et al., 2020; Vrtička and Vuilleumier, 2012). In this model, the affective system can be further separated into subsystems called the aversion module (consisting of activation of the ACC, insula, hippocampus/HPA axis, amygdala and anterior temporal pole) and the approach module (consisting of activation of the ventromedial prefrontal/orbitofrontal cortex (OFC), ventral striatum, hypothalamus and ventral tegmental area/substantia nigra) (Long et al., 2020; Vrtička and Vuilleumier, 2012). The neural activity between these modules has been proposed to be influenced by various neurotransmitters and hormones, including: dopamine, oxytocin, serotonin, cortisol, androgens/estrogen, and endogenous opioids (Long et al., 2020; Vrtička, Sander, et al., 2012). Furthermore, this model divides the cognitive system into subsystems called the emotional regulation module (involving the activation of the dorsolateral prefrontal cortex and lateral OFC) and the mental state representation module (involving the activation of the medial prefrontal cortex, posterior cingulate cortex/precuneus, posterior superior temporal sulcus/temporo-parietal junction, anterior superior temporal gyrus and fusiform gyrus) (Long et al., 2020; Vrtička and Vuilleumier, 2012).

Each subsystem of the neurophysiological model of the attachment system governs the presentation of specific behaviours when the attachment system is activated in response to a threat (Vrtička and Vuilleumier, 2012). The affective system's aversion module is proposed to be activated when processing physical and social threats, resulting in the presentation of withdrawal behaviours and defense responses (Vrtička and Vuilleumier, 2012). The affective system's approach module is also proposed to be activated in response to physical and social threat, but in promotes social interaction and behaviours that encourage proximity with others as a way of counteracting the threat (Vrtička and Vuilleumier, 2012). For securely attached individuals, the aversion and approach modules are proposed to be in balance with one another to ensure a healthy response to physical and social threats (Vrtička and Vuilleumier, 2012).

The cognitive system's emotional regulation module has been proposed to be activated when unconsciously processing physical information from others (such as body language and facial expressions), resulting in the presentation of adaptive emotional responses (Vrtička and Vuilleumier, 2012). When there is a decreased activation of the emotional regulation module, it has been suggested to result in either exaggerated emotional responses (anxious attachment) or stunted emotional responses (avoidant attachment) (Vrtička and Vuilleumier, 2012). Lastly, the cognitive system's mental state representation module has been proposed to be activated when consciously processing physical social cues, resulting in the analysing of internally-focused information about others (such as intentions and mental states) (Vrtička and Vuilleumier, 2012). Therefore, based on limited evidence, researchers propose that the activation of these brain subsystems, and subsequent presentation of behaviours, differs depending on an individual's adult attachment style (Long et al., 2020). The proposed model representing the neurophysiological activation of the attachment system is summarised in Figure 1.4.

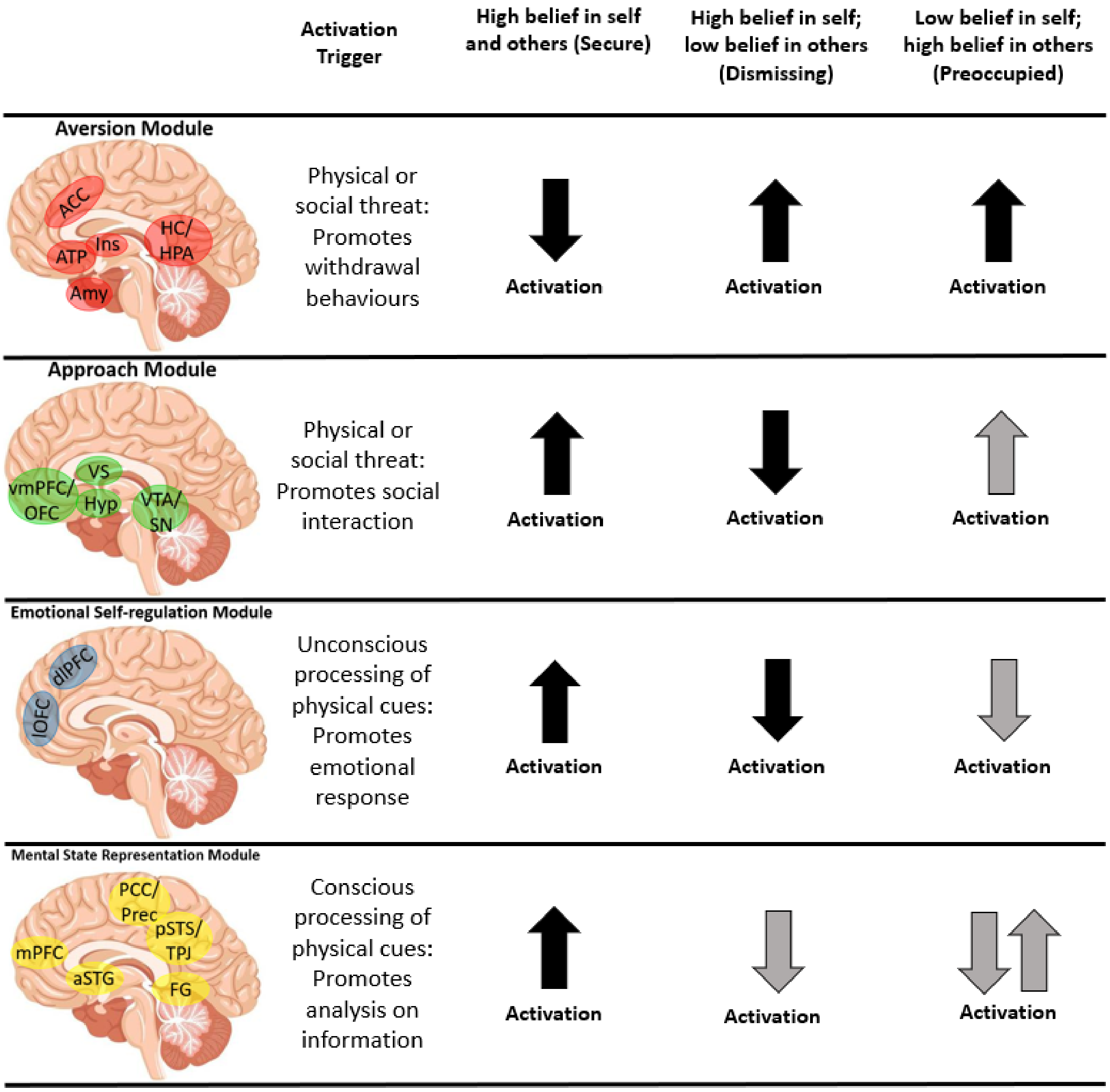

Figure 1.4: A summary of proposed module activation in response to threat in the neurophysiological model of the adult attachment system, adapted from Vrtička and Vuilleumier (2012) and Long *et al.* (2020). *Upward-pointing arrows represent increased activation while downward-pointing arrows represent decreased activation. Black arrows are used to show that there is considerable evidence to support the proposed module activation for the specific adult attachment style. Grey arrows are used to show that there is little evidence to support the proposed module activation for the specific adult attachment style. ACC = anterior cingulate cortex, INS = insula, HC/HPA = Hippocampus/HPA-axis, AMY = amygdala, ATP = anterior temporal pole, VS = ventral striatum, vmPFC/OFC = ventromedial prefrontal cortex/orbitofrontal cortex, HYP = hypothalamus, VTA/SN = ventral tegmental area/substantia nigra, lOFC = lateral orbitofrontal cortex, dlPFC = dorsolateral prefrontal cortex, mPFC = medial prefrontal cortex, PCC/PREC = posterior cingulate cortex/precuneus, aSTG = anterior superior temporal gyrus, pSTS/TPJ, posterior superior temporal sulcus, temporo-parietal junction, FG = fusiform gyrus.*

The neural structures governing certain support-seeking or aversion behaviours in times of threat are potentially created through a learned response based on prior interpersonal interactions in times of threat (Bosmans et al., 2020). It has been suggested that a Secure attachment style develops in a similar manner to the safety conditioning learning process. An attachment figure may act as a safety cue that, through a learning response of safety, may inhibit fear and stress responses through the release of dopamine when the safety cue is present (or perceived to be available) (Bosmans et al., 2020). In Insecure adult attachment styles, the attachment figure is not perceived as a safety cue, and the fear response is perpetuated instead of inhibited (Bosmans et al., 2020). Importantly, the brain regions that have been found to be involved in adult attachment overlap with many of the brain regions involved in pain and in placebo analgesia (Figure 1.5).

1.6 Adult attachment and pain

Studies using functional magnetic resonance imaging (fMRI) and electroencephalograms (EEG) demonstrate that activity in core brain areas involved in the activation of the attachment system largely overlap with those during pain and expectation-induced placebo analgesia (Figure 1.5) (Long et al., 2020; Vrtička, Bondolfi, et al., 2012; Vrtička et al., 2008). For example, secure attachment (high belief in the self and others) requires symmetric prefrontal cortex function (Gander and Buchheim, 2015); specifically, the dorsolateral prefrontal cortex (dlPFC, Figure 1.5), which plays a significant role in expectation-induced placebo analgesia (Krummenacher et al., 2010). The dlPFC (together with the hippocampus: key area for learning and memory (Voss et al., 2017)) attaches context and meaning to an experience, providing information on how a present experience relates to the past, and how it might affect the future (Pascual-Leone et al., 1996; Rao et al., 1997). With specific reference to pain, one study demonstrated how auditory cues, used to elicit expectation of pain, influenced heat-evoked responses in the key pain-processing regions (Atlas et al., 2010). The effects on several brain regions, including the insula and medial OFC, correlated with pre-task expectations, supporting that expectancy plays a prominent role in the perception of pain. Moreover, the same study found that a subset of pain-processing regions, including the ACC, anterior insula, and thalamus, are affected by cue-evoked anticipatory activity in the medial OFC and ventral striatum. In turn, these pain processing regions mediate expectation-induced effects on activated brain regions involved in processing pain (Atlas et al., 2010; Mao et al., 2020). The authors, therefore, suggest that activity in pain-processing regions reflects a combination of nociceptive input and top-down information related to expectations, and that anticipatory processes in the OFC and striatum may be important in modulating pain processing (Atlas et al., 2010). Accordingly, the brain areas involved in expectation-induced pain perception and placebo analgesia overlap considerably with brain areas that show increased activation during support seeking behaviours (e.g. OFC) and emotional self-regulation and mental representations of past social interactions (e.g. dlPFC) (Long et al., 2020) (Figure 1.5).

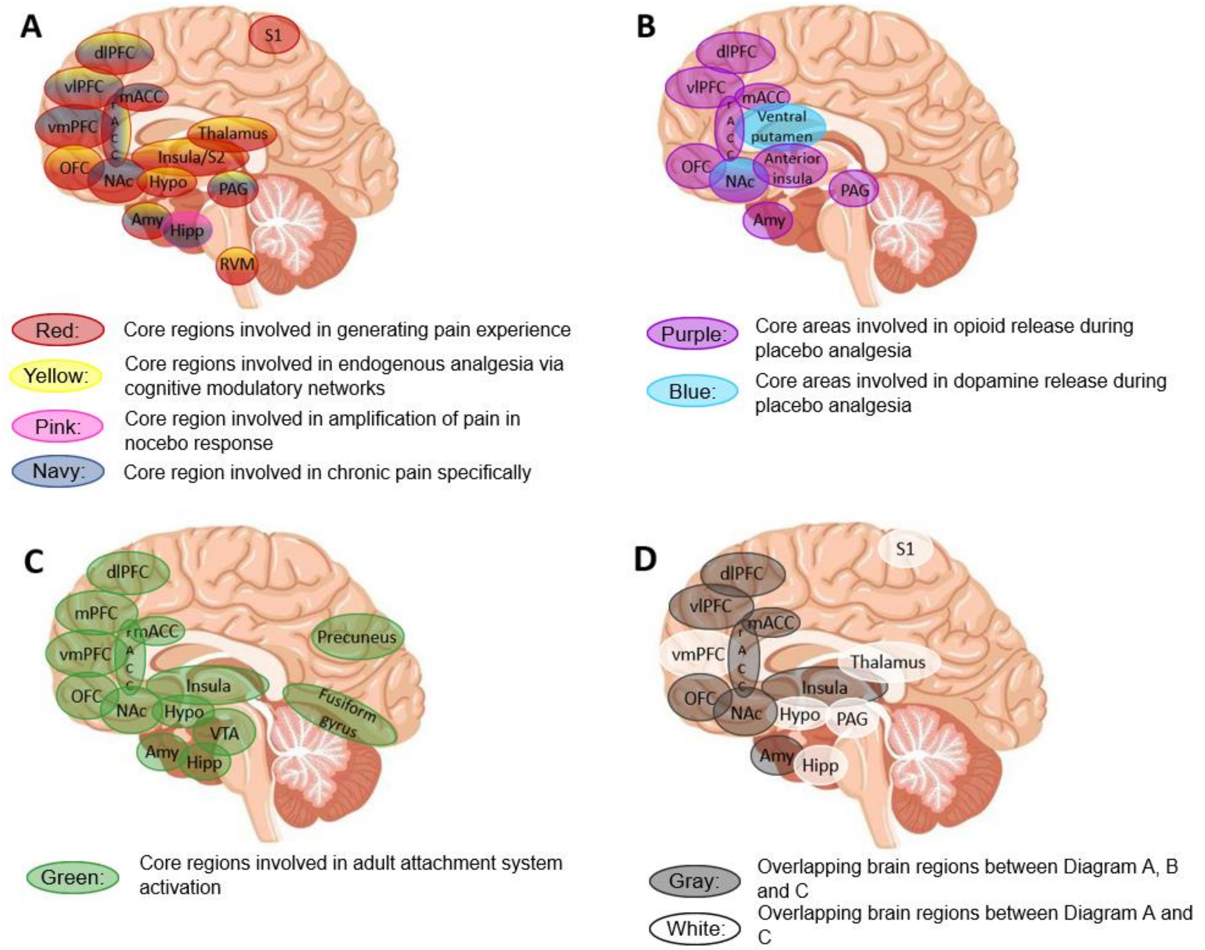

Figure 1.5: Schematic illustration of the brain regions involved in experience pain (A), placebo analgesia (B) and the adult attachment system in times of threat (C) and overlap of the regions involved in pain, placebo analgesia and attachment (D). *Diagram A highlights the core brain regions involved in pain (red). The yellow regions overlap with some of the red regions, specifically showing core brain regions involved in endogenous analgesia via cognitive modulatory networks. Cognitive factors that impact these networks include, among others: expectation, reappraisal, attention, beliefs learning and conditioning, emotions such as anxiety and depression. The hippocampus (pink) plays a role in the amplification of the pain experience which occurs during nocebo responses and with increased levels of anxiety (Tracey, 2010). Diagram A also highlights the core regions involved in chronic pain specifically (navy)* (Yang and Chang, 2019). *Diagram B highlights the core brain regions involved in placebo analgesia. Specifically, the purple areas are the key regions involved in releasing opioids during placebo analgesia, and blue areas are the key regions involved in releasing dopamine during placebo analgesia. The NAc releases both opioids and dopamine in a bidirectional response manner where increased release is induced in the placebo response while decreased release is induced during a nocebo response (Tracey, 2010). Diagram C highlights the core brain regions involved in the activation of the adult attachment system in times of threat (green). The way in which these brain regions have increased or decreased activation depends on the adult attachment style, but diagram C summarises the regions involved when the*

attachment system is stimulated in response to threat (Long et al., 2020). Diagram D highlights the overlapping brain regions involved in pain, placebo analgesia and the adult attachment system (grey) and the overlapping brain regions involved in pain and adult attachment (white). dlPFC = dorsolateral prefrontal cortex, vlPFC = ventrolateral prefrontal cortex, vmPFC = ventromedial prefrontal cortex, OFC = orbitofrontal cortex, rACC = rostral anterior cingulate cortex, mACC = midanterior cingulate cortex, NAc = nucleus accumbens, S1 = primary somatosensory cortex, S2 = secondary somatosensory cortex, Hypo = hypothalamus, Amy = amygdala, Hipp = Hippocampus, PAG = periaqueductal grey, RVM = rostral ventromedial medulla, mPFC = medial prefrontal cortex, VTA = ventral tegmental area.

1.6.1 Adult attachment and experimental pain

To my knowledge there are only 10 studies looking at the association between adult attachment and experimental pain (Andrews et al., 2011; Hurter et al., 2014; Krahé et al., 2015, 2016; MacDonald, 2008; Meredith et al., 2006a; Mohr et al., 2018; Rowe et al., 2012; Sambo et al., 2010; Wilson and Ruben, 2011). One of these studies, on 58 healthy male and female participants, was conducted without specifically altering, or controlling for, the social context and simply looked at the association between adult attachment and pain threshold, tolerance and intensity (Meredith et al., 2006a). This study found that an increased attachment anxiety (low belief in self) was associated with a decreased pain threshold when compared to low attachment anxiety. No associations were found with the attachment avoidance (belief in others) dimension (Meredith et al., 2006a). All other studies investigating the association between adult attachment and experimental pain have done so in a variety of orchestrated social contexts. The study design and results of these studies are summarised in Table 1.1. There have also been two recent studies investigating how the association between experimentally induced secondary hyperalgesia and social support is moderated by adult attachment dimensions (Jaltare et al., 2023, 2024). The results from these studies with similar protocols are, however, contradictory. One study found that attachment avoidance was associated with overall lower secondary hyperalgesia and a smaller area of secondary hyperalgesia, but no moderating effects by adult attachment between secondary hyperalgesia and physical social support (via handholding) were found (Jaltare et al., 2023). Conversely, the most recent study found that both attachment anxiety and avoidance dimensions moderated the association between low secondary hyperalgesia and the presence of verbal social support (Jaltare et al., 2024). These conflicting results may be due to the different forms of social support (physical versus verbal) but calls for further research on the effect of adult attachment on the relationship between social support an experimentally induced secondary hyperalgesia.

Table 1.1: A summary of studies investigating the effects of different social contexts (affective touch, empathy and social threat) on pain perception according to belief in the self and belief in others.

Reference	Population and sample size	Study design (how social context was manipulated) and study aims	Results	Critique in line with attachment research
MacDonald (2008)	88 (Experiment 1) and 50 (Experiment 2) healthy adult male and female participants (mean age of 21). 82% of sample was female.	The study consisted of two separate experiments that took part at different times and with different participants. Both experiments were investigating the effect of social exclusion on the perception of pain intensity. Each experiment was double-blinded, and participants were randomly divided into two groups (inclusion/control or exclusion). Participants volunteered to partake in both experiments and were not made aware of the true purpose of the study. In the first experiment, social exclusion/inclusion was modeled by participants playing an online ball toss game with, what the participants were made to believe, were real people. The participants were either excluded from the game (exclusion group receiving	Participants who had higher baseline cold pain thresholds and low belief in self, were found to maintain a high pain threshold after the exclusion task (in both experiments). Individuals with a high belief in self and high pre-exclusion thresholds were found to have decreased thresholds after the exclusion tasks (in both experiments). No similar relationships were found with the belief in others attachment dimension, suggesting that the relationship between high baseline threshold and the threshold post manipulation only depended on levels of belief in self. The author suggests that these results demonstrate how individuals with a low belief in self have increased pain thresholds in an	The presence of an association (between low belief in self and high pain threshold after exclusion) for the low belief in self dimension but not the low belief in others dimension makes sense in the context of attachment literature. Individuals with a low belief in self look towards others when they perceive a threat, so the presence and quality of the external support is important. Individuals with a low belief in others prefer to rely on themselves during times of threat and, as such, the presence and quality of social support is likely to be of less importance when

		few ball tosses) or were included in the game (control group receiving similar amounts of ball tosses as the other players). The second experiment modeled social exclusion by either asking the participants to write about a past experience of social rejection (exclusion groups) or about emotions that arise when watching television (inclusion/control group). In both these experiments, participants underwent a cold pressor test before and after the social exclusion and their adult attachment style was determined and represented in terms of the attachment dimensions of anxiety and avoidance.	attempt to appear less vulnerable in a situation where they fear that rejection is likely.	evaluating and responding to a threat (Mikulincer and Shaver, 2003, 2007).
Sambo et al. (2010)	30 healthy male and female adult participants (mean age of 29). 67% of sample was female.	This study investigated the effect of perceived empathy from an unknown observer on the relationship between adult attachment and experimental pain perception. They used thermal noxious stimuli administered by placing a thermode on the volar surface of the participant's	This study reported that individuals who had a low belief in self reported less pain when a high-empathy compared to a low-empathy unknown observer was present. Individuals who had a low belief in others reported less pain when alone compared to in the presence of an	Individuals with a low belief in self are likely to feel safer if the support they receive from others appears readily available, like in the case of high empathy. Individuals with a low belief in others are likely to feel safest on their own during a perceived threat since they distrust external

		forearm. An unknown observer was present when the threshold was determined for the participant. Before the experimental phase when participants rate their pain intensity, the experimenter told the participant (in the absence of the observer) whether the observer reported high or low empathy. For the experimental phase, the observer was either present (after having reported high or low empathy) or absent (control condition). All participants participated in each empathy condition and the order of the conditions was randomised.	observer, regardless how empathetic the observer was.	support (Mikulincer and Shaver, 2003, 2007).
Andrews et al. (2011)	82 healthy male and female adult participants (mean age of 24). 44% of sample was female.	A cold pressor test was conducted on each participant to investigate how the relation of the experimenter to the participant (whether the experimenter was known or unknown to the participant) affected the association between adult attachment and pain when controlling for personality traits.	When the participant was a friend or family member of the experimenter, individuals who had a high belief in self but a low belief in others (dismissing attachment) reported decreased pain intensities and increased pain tolerances compared to when the experimenter was unknown, suggesting an effect of social environment on pain.	When considering the role of attachment figures (Bowlby, 1969; Mikulincer and Shaver, 2007) in creating safety, it follows that individuals with a low belief in others would still feel safer with people they know. However, the lack of association with the low belief in self dimension and whether the experimenter was

				known or unknown is potentially puzzling because these individuals would also likely feel safer (thus reporting lower pain intensities) in the presence of the known experimenter compared to the unknown experimenter.
Wilson and Ruben (2011)	65 healthy females in a committed heterosexual relationship (mean age of 20).	The purpose of the study was to assess the relationship between adult attachment and reported pain measures of threshold, tolerance and intensity and with pulse rate (a measure of physiological arousal). A blood pressure cuff was placed around the participant's upper arm and inflated. The participants performed hand grip exercises to induce ischaemic pain in the presence of their romantic partner.	This study found that women with higher attachment anxiety (low belief in self) showed lower pain thresholds and greater subjective pain during an ischemic pain task compared to the women with low attachment anxiety (high belief in self). Moreover, avoidantly (low belief in others) attached women showed lower pain thresholds and tolerances in the presence of higher attachment anxiety (low belief in self) partners, whereas the securely attached women showed the opposite pattern. Lastly, higher avoidance (low belief in others) was linked to significantly lower pulse rates during the pain task, even at peak pain points.	This study emphasises the effect that romantic partners' attachment styles can have on the perception of pain, where having a romantic partner with a low belief in self during a painful experiment may not reduce, and may perhaps even increase, the perceived threat of the situation despite the presence of the attachment figure.

Rowe et al. (2012)	95 healthy male and female adult participants (mean age of 22). 61% of sample was female.	The study aimed to investigate the association between Anxious and Secure attachment priming and pain sensitivity. Participants underwent two cold pressor tests, during which they reported their pain threshold and tolerance. The first test was performed prior to attachment priming. The second test was performed 10 minutes after the first test, following an attachment priming procedure. The attachment priming procedure involved the participants either writing about a relationship that they felt secure and comfortable with (Secure priming) or a relationship where they felt that the other person did not get as close to the participant as they would have liked them to (attachment anxiety priming).	This study found that participants' pain threshold and tolerance increased in the second cold pressor test compared to the first cold pressure test regardless of whether the participants were primed for a Secure or Anxious attachment. There was no difference in the pain thresholds or tolerances between the two attachment prime groups for the second cold pressor task.	No difference between the groups may have been due to the use of attachment priming rather than inherent attachment styles.
Hurter et al. (2014)	54 healthy male and female adult participants in	The study aimed to investigate the effect of perceived empathy from a romantic partner on the relationship	When a highly empathetic romantic partner was present, individuals with a high belief in others reported more	The results from this study are paradoxical to attachment research. A high belief in others

	long term (>1 year) relationships (mean age of 24). 52% of sample was female.	between adult attachment and experimental pain perception. They used two separate cold pressor tests for the noxious experimental stimulus, conducted on separate hands. Two cold pressor tests were used to investigate two empathy conditions (high and low empathy). The order of the empathy manipulation was randomised for each participant. For each cold pressor test, the observing partner was asked to rate the empathy they felt for the participating partner. After the participating partner signaled their pain threshold, the experimenter falsely reported the empathy of the observing partner (either reported it as high or low) to the participating partner. The effect of the perceived empathy on pain tolerance for the different adult attachment styles was investigated.	pain compared to those who had a low belief in others. There was no difference in pain perceptions among the adult attachment styles for the low empathy group.	means increased trust in others' abilities to offer support during a threatening situation (Mikulincer and Shaver, 2007). As such, a higher empathy partner present when these individuals undergo the experimental procedure would be expected to result in lower reported pain intensities compared to high empathy observers for individuals with low belief in others. The pain intensity rating were also not verbal so are unlikely to reflect individuals attempting to seek support.
Krahé et al. (2015)	39 healthy female adult participants in a committed	The study aimed to investigate the effect of perceived empathy from a romantic partner on the relationship	Individuals with low belief in others reported lower pain intensities when their partners were absent compared	Individuals with a low belief in others are unlikely to trust in the support offered and tend to rely

	(over a year) heterosexual relationship (mean age of 26). All participants were right-handed.	between adult attachment and experimental pain perception. A laser-evoked radiant heat stimulus was applied to the dorsal digits of the left hand as the experimental noxious stimulus. Participants underwent the noxious stimulus procedure three times. In one condition, the romantic partner was asked to rate their empathy for their partner's pain (they were focused on the partner). In the second condition, the romantic partner was asked to rate their empathy for another participant's pain who was undergoing the procedure in the same room (they were focused on someone else). The third condition required the romantic partner to leave the room to rate the empathy for another participant's pain in a different room (they were absent). The order of the conditions was randomised.	to present during the experimental pain procedure. No associations with the belief in self attachment dimension were found.	on themselves during times of perceived threat (Mikulincer and Shaver, 2007). Following the same attachment logic, the lack of association for the low belief in self dimension is unexpected since these individuals would be expected to feel less safe when trying to cope with a perceived threat alone compared to if there was a possibility of external support (Mikulincer and Shaver, 2007).
Krahé et al. (2016)	50 healthy female adult participants	The study aimed to investigate the effect of affective touch (with a makeup	When the affective touch was administered to participants with a low	This study suggests fast touch is potentially perceived as a safety

	(mean age of 24). All participants were right-handed.	brush) administered by a stranger on the relationship between adult attachment and experimental pain perception. They used laser-evoked radiant heat stimuli applied to the dorsum of the left digits as the experimental noxious stimulus. The affective touch was applied to the forearm in one group of participants and to the palm of the other group of participants. Within each group, the affective touch was administered both with a fast and slow velocity and the order of velocities was randomised. Affective touch was administered to the contralateral hand to the laser stimulus.	belief in self, fast touch was associated with decreased pain intensities compared to slow touch. Individuals with a low belief in others were found to perceive decreased pain intensities when slow (compared to fast) affective touch was administered.	cue when there is a low belief in self, whereas slow touch may potentially be a safety cue for individuals with low belief in others. It is unclear why this would be the case when looking at attachment concepts.
Mohr et al. (2018)	32 healthy female adult participants in a committed (over a year) heterosexual relationship (mean age of 25). All participants	The study aimed to Investigate the effect of affective touch (with a makeup brush) administered by a romantic partner on the relationship between adult attachment and experimental pain perception. Affective touch was administered to the contralateral hand to the laser stimulus.	Affective touch administered to individuals with a low belief in self by their romantic partner showed that there was no difference in the pain ratings for fast or slow touch. Individuals with higher belief in self showed significantly increased pain ratings with fast compared to slow affective touch.	The conflicting results between this study and the previous one (Krahé et al., 2016) suggests that the effect of types of affective touch as potential safety cues during the pain procedure is inconclusive.

	were right-handed.	They used a laser-evoked radiant heat stimulus applied to the dorsum of the left hand as the experimental noxious stimulus. Affective touch was administered both with a fast and slow velocity to the participant's forearm (the order of the velocities was randomised).	There was no relationship between the belief in others attachment dimension and pain ratings for either fast or slow affective touch.	

The studies summarised in Table 1.1 provide evidence of an association between adult attachment and experimental pain. Taken together, there are some broad relationships between the adult attachment dimensions of belief in self and others and experimental pain. Individuals with a low belief in self reported reduced pain intensities when in the presence of a high (compared to low) empathy stranger (Sambo et al., 2010) but increased pain thresholds when being socially excluded (compared to included) (MacDonald, 2008) during the pain procedure. In the context of attachment literature, these results emphasise the weight that individuals with a low belief in self place on others when under a perceived threat (Mikulincer and Shaver, 2007). Should the support of others seem likely (high empathy), then individuals with a low belief in self may be more likely to feel safe and report reduced pain intensities. On the other hand, if support from others seems unlikely (social exclusion), individuals with a low belief in self may raise their pain tolerance so as not to appear weak in a social context where they do not feel safe. For individuals with a low belief in others, the studies from Table 1.1 collectively show reduced pain intensities reported when these individuals were alone compared to in the presence of either a stranger (Sambo et al., 2010) or a romantic partner (Krahé et al., 2015) during the experimental pain procedure. These individuals also reported reduced pain intensities and higher pain tolerances when the researcher was known compared to unknown (Andrews et al., 2011). In line with attachment literature, individuals with a low belief in others are unlikely to seek support and feel safer on their own (Mikulincer and Shaver, 2007). Importantly, these individuals will still feel safer in the presence of a known figure compared to an unknown one, emphasising the importance of attachment figures. However, likely due to varied methodologies and social contexts, no consistent pattern of association (or lack thereof) between adult attachment style and experimental pain can be truly identified.

1.6.2 Adult attachment and chronic pain

Previous literature has shown evidence of an association between adult attachment and chronic pain. Studies have shown that more than half (up to 65%) of individuals with chronic pain have an Insecure adult attachment style (Andersen, 2012; Belot et al., 2021; Davies et al., 2009; Kowal et al., 2015; Nasika et al., 2023). Moreover, responses to chronic pain rehabilitation programmes (Andersen, 2012; Kowal et al., 2015), health seeking behaviours (Belot et al., 2021; Ciechanowski et al., 2003) and general coping strategies for chronic pain, including self-compassion and self-efficacy (Ciechanowski et al., 2003; Meredith et al., 2006b; Nasika et al., 2023) differ between securely and insecurely attached individuals with chronic pain. The following paragraphs summarise some of these studies in more detail, highlighting the importance of considering adult attachment style in the possible treatment of chronic pain.

A longitudinal study was conducted on 235 patients who formed part of an outpatient chronic pain self-management rehabilitation programme (Kowal et al., 2015). This study found that, at baseline, the frequency of Insecure attachment styles in people with chronic pain was significantly higher (65.5%) than the frequency of the Secure adult attachment style in people with chronic pain (34.5%). Of the insecurely attached patients with chronic pain, most were of the Dismissing (29.4%) and Fearful (24.3%) styles, and 11.9% had a Preoccupied adult attachment style (Kowal et al., 2015). The high prevalence of Insecure adult attachment styles in these patients was proposed to suggest either that chronic pain reduces the quality of relationships with attachment figures, or that insecurely attached individuals, with their attachment likely stemming from their infant attachment style, are less effective in managing their pain over time, thus resulting in the development of chronic pain, possibly due central sensitisation to pain (Kowal et al., 2015). Alternatively, the high frequency of insecurely attached people with chronic pain may be due to the association between insecure attachment styles and psychological factors (depression, anxiety and pain catastrophising) previously shown to be associated with and exacerbate chronic pain (Lerman et al., 2015; Meredith et al., 2006b; Petrini and Arendt-Nielsen, 2020; Rajkumar, 2022). Either way, Insecure adult attachments were more prevalent over Secure attachment, in individuals with chronic pain (Kowal et al., 2015).

One study statistically assessed the prevalence of adult attachment styles in individuals with chronic widespread pain compared to those with no pain (Davies et al., 2009). This cross-sectional population based study, on individuals registered at three separate general practices in north-west England, was conducted to investigate the relationship between adult attachment styles and chronic widespread pain (defined as chronic pain occurring in at least two contralateral areas below and above the waist for three months or longer) (Davies et al., 2009). Of the total of 1361 participants, 18.4% reported chronic widespread pain, and the participants with chronic widespread pain were 70% more likely to be classified with an Insecure adult attachment style compared to the participants who did not have chronic widespread pain (Davies et al., 2009). Moreover, an observational study involving 101 patients from a headache clinic reported that Insecure adult attachment styles were more common (66%, 34/99) in individuals presenting with migraines to a neurology clinic than healthy controls (50%, 2227/4454) (Belot et al., 2021). As such, both studies highlight the increased prevalence of Insecure adult attachment styles in individuals with chronic pain, possibly suggesting that an Insecure adult attachment style may be a risk factor for the development of chronic pain.

While an Insecure attachment style is more prevalent in individuals with chronic pain, the association between chronic pain prevalence and attachment style is still statistically unknown albeit likely. Moreover, it seems that attachment style may associate only with pain prevalence, and not pain intensity or pain-related disability (Andersen, 2012; Davies et al., 2009; Kowal et al., 2015; Meredith et al., 2006b). In two studies assessing the physical (chronic pain intensity and chronic pain-related disability) and psychological outcomes (pain catastrophising, self-efficacy, anxiety and depression) of chronic pain patients following a pain rehabilitation programme, both the insecurely and securely attached individuals showed improvement in their reported pain intensity and functional status (a measure of pain-related disability) of their chronic pain from baseline to completion of the programme. However, no differences were found in the level of improvement for chronic pain intensity or chronic pain-related disability between the two groups upon completion of the programme (Andersen, 2012; Kowal et al., 2015). Nevertheless, Insecure attachment styles have been found to associate with an increased number of pain sites when compared to Secure attachment (Davies et al., 2009), suggesting a possible increased vulnerability to chronic pain in insecurely attached.

Supporting the notion of a vulnerability of insecurely attached individuals (as determined by increased attachment anxiety and/or avoidance) to chronic pain, is evidence that these individuals show poorer improvements in depression, pain catastrophising and self-efficacy when compared to securely attached individuals, following the completion of pain management programmes (Ciechanowski et al., 2003; Kowal et al., 2015; Meredith et al., 2006b, 2007). One study found that the Dismissing attachment style was associated with higher levels of anxiety, and the Preoccupied and Fearful attachment styles were associated with poorer self-efficacy when compared to the Secure attachment group (Meredith et al., 2006b). These results are in line with attachment theory where Preoccupied and Fearful attachment styles are characterised by a decreased belief in self (Mikulincer and Shaver, 2007), suggesting that self-efficacy would likely be impacted in these individuals when dealing with a perceived threat. Moreover, higher levels of anxiety and poorer self-efficacy were associated with increased pain severity and disability, particularly when accompanied by high attachment anxiety (Meredith et al., 2006b), emphasising the role that the psychological factors of pain play in affecting chronic pain severity and related disability and thus the importance of considering adult attachment styles due to their association with these same psychological variables.

When looking at the attachment dimensions, other studies have found that high attachment anxiety (low belief in self) was associated with increased post-treatment depression and decreased post-treatment self-efficacy when compared to low attachment anxiety (Kowal et al., 2015; Meredith et al., 2007). High attachment avoidance (low belief in others) was also found to associate with increased post-treatment depression as well as increase post-treatment pain catastrophising when compared to low attachment avoidance (Kowal et al., 2015; Meredith et al., 2007). Another study by the same authors also found that both a high attachment anxiety and high attachment avoidance dimensions were correlated with increased depression, both before and after treatment (Meredith et al., 2007). Even in a study that found statistically significant improvements in pain intensity and opioid use for the Insecure attachment following a pain rehabilitation programme, the study concluded that these improvements were not clinically relevant to claim successful rehabilitation of the Insecure group compared to the Secure group (Andersen, 2012). It follows that proposed reasons why individuals with Insecure attachment styles make up the majority of chronic pain populations may, therefore, be due to a greater prevalence of other factors associating with chronic pain including depression, anxiety, pain catastrophising and self-efficacy (Andersen, 2012; Ciechanowski et al., 2003; Kowal et al., 2015; Meredith et al., 2006b, 2007).

Taken together, these studies demonstrate that although there is no direct association between adult attachment and chronic pain burden, the literature shows that individuals with an Insecure adult attachment style are not being effectively rehabilitated due poor psychological health outcomes following the completion of chronic pain management programmes (Andersen, 2012; Kowal et al., 2015; Meredith et al., 2007). I propose that the concept of threat and threat appraisals may be a common thread; as the influence of threat on both pain and on attachment style appears frequently in literature, as discussed in this chapter (Boston and Sharpe, 2005; Kim et al., 2020; Todd et al., 2016; Van Vliet et al., 2021; Vrtička, Sander, et al., 2012; Vrtička and Vuilleumier, 2012; Wang et al., 2016). Looking at threat as a common thread between pain and adult attachment may provide an avenue to explore mechanisms to explain the complex relationship between these two factors, improving the understanding of chronic pain in the context of interpersonal relationships. It is, however, important to acknowledge that threat appraisal is influenced by other additional factors such as personality (Tomaka and Magoc, 2021) and emotional intelligence (Mikolajczak and Luminet, 2008). That being said, adult attachment anxiety and avoidance dimensions are positively correlated with personality traits of neuroticism (Noftle and Shaver, 2006), which is also associated with high tendency to appraise a threat (Tomaka and Magoc, 2021). Additionally, while individuals with a low emotional intelligence are more likely to appraise a situation as a threat compared to those with a high emotional intelligence (Mikolajczak and Luminet, 2008), insecure adult attachment styles are characterised by decreased emotional regulation (Long et al., 2020; Mikulincer and Shaver, 2007). As such, it seems likely that adult attachment may be a confounding factor in the relationship between threat appraisal and both personality and emotional intelligence, emphasising the importance of considering attachment and its link to threat in pain research.

1.7 Conclusion

This literature review has underscored the subjective nature of pain and its intricate relationship with various psychosocial factors. It has been demonstrated in the overlap of brain areas involved in pain modulation, placebo analgesia and the adult attachment system. Emphasis has been placed on threat as a linking factor between adult attachment styles and the perception of pain by discussing how expectations and learnt experiences affect the perception of pain and the formation of attachment styles. By understanding how attachment styles influence individuals' responses to threats, like pain, we might gain a deeper understanding of the interpersonal dynamics surrounding pain.

This review has, however, also highlighted that the association between adult attachment and pain is unclear due to the methodological designs used to date. For example, studies on experimental pain an adult attachment use different methods of inducing pain and of controlling or manipulating the social context. While there is evidence of an association between adult attachment and experimental pain, no clear or consistent relationship can be identified from the current literature due to the methodological inconsistencies in the literature. Moreover, while evidence suggested that individuals with Insecure attachment styles are more vulnerable to developing chronic pain, there are no studies looking at chronic pain prevalence for attachment styles in a general population.

In conclusion, understanding how the activation of the adult attachment system in response to perceived threat alters an individual's pain perception could substantially enhance our comprehension of pain as a social phenomenon and inform the development of more effective treatment strategies. By examining the influence of attachment styles on pain perception, a more comprehensive understanding of the interpersonal dynamics that shape pain experiences can be gained. This knowledge has the potential to enhance pain management strategies, optimise treatment outcomes, and ultimately improve the overall well-being of individuals suffering from pain. By addressing pain not only as a physical sensation but also as a social phenomenon, it may pave the way for more effective and holistic approaches to pain assessment, intervention and care.

1.8 Thesis aims

There is evidence that individuals with chronic pain are more likely to have an Insecure adult attachment rather than a Secure adult attachment. The vulnerability of insecurely attached individuals with chronic pain has, therefore, been highlighted in the literature, but no study has directly evaluated whether a relationship between adult attachment style and chronic pain prevalence exists. As such, my first aim is to determine the association between adult attachment style and chronic pain prevalence in a general cohort. I begin my thesis by addressing this aim through the following objectives in Chapter 3, all with reference specifically to a general South African cohort obtained through a nationwide online survey:

1) Is there an association between adult attachment style and chronic pain prevalence?
2) Is there an association between adult attachment style and the burden (chronic pain intensity, interference and number of chronic pain sites) of chronic pain?

While less studied, there is also evidence of an association between experimental pain and adult attachment styles, although no consistent trend can be determined from the current literature. Moreover, there are currently no studies researching the possible relationship between adult attachment style and methods of endogenous analgesia as a way of examining possible mechanisms for the development of chronic pain in insecurely attached individuals. As such, my next aim is to determine the association between adult attachment and experimental pain measures, both static and dynamic, in females. The reason I chose to use a female-only sample is due to known sex differences in pain reporting (Myers et al., 2003; Wiesenfeld-Hallin, 2005). Although the data on sex differences are inconsistent (Racine et al., 2012), I chose to include only females to minimise potential confounding effects, especially considering there is currently no baseline for this research. Furthermore, experimenter gender can influence pain perception (Levine and De Simone, 1991). As I, the experimenter, am female, recruiting females ensured consistency in this aspect (Levine and De Simone, 1991). I met my aim by addressing the following objectives in Chapter 4, all with reference to a healthy, pain-free and female cohort who participated in an experimental pain study:

1) Is there an association between adult attachment style and static measures of experimentally induced thermal pain (pain threshold, tolerance and single-point intensity)?
2) Is there an association between adult attachment style and cumulative pain load from contact heat?

3) Is there an association between adult attachment style and the Conditioned Pain Modulation effect as a method of measuring a pathway of endogenous pain inhibition (another dynamic measure of pain)?

In Chapter 5, I integrate the findings from both the survey and experimental pain studies and discuss the importance of considering adult attachment style in pain research together with possible implications and directions for future studies in the field of adult attachment and pain.

CHAPTER 2

METHODS

2.1 Methods overview

My research was divided into two parts to address each main aim. To determine whether there is an association between adult attachment style and chronic pain prevalence (first aim) in a general population, I conducted a nationwide online survey (Part 1). The second aim of this thesis was to determine whether there was an association between adult attachment style and experimental measures of pain (pain threshold, tolerance and intensity) and endogenous analgesia (conditioned pain modulation). To address this second aim, Part 2 of my research made use of an experimental procedure involving the testing of static (heat pain threshold, tolerance, single-point intensity) and dynamic (cumulative pain load and CPM as a method of measuring endogenous analgesia) measures of pain.

I required all participants in Part 2 to complete the same questionnaire as those who participated in the survey from Part 1 before participating in the experimental procedure, because the survey contained questionnaires assessing important information needed in both parts of the study (demographic data, adult attachment style, depression, anxiety, stress, and pain catastrophising).

2.1.1 Ethical clearance

The thesis protocol was approved by the University of the Witwatersrand's Human Research Ethics Committee (Medical), which adheres to the principles of the Declaration of Helsinki and the Declaration of the World Medical Association (clearance certificate number: M210449 (Part 1) (Appendix 1); M211003 (Part 2) (Appendix 2)).

2.1.2 Ethical considerations

To ensure that all participants in both parts of my thesis research had full autonomy, information sheets for both the online survey (Appendix 3) and the CPM procedure (Appendix 5) were provided. The information sheets included information regarding their respective procedures as well as the global purpose of the study. Additionally, the information sheets for both the survey and the CPM experimental procedure made it clear that participation was completely voluntary, and participants could choose to leave the study at any point without repercussions and with no explanation needed.

For Part 2, I also went over the full CPM procedure with each participant and asked if there were any questions before handing over the consent form for them to read and fill out.

There were no benefits or risks associated with participating in the survey. For the CPM procedure, the information sheet fully disclosed potential risks and benefits for the participants. More specifically, the information sheet stated that participants may feel discomfort or pain during the procedure and, for a few minutes following the completion of the procedure, but that none of the stimuli used in the protocol would cause any tissue damage or harm to the participant. The information sheet also made it clear that participants would not benefit directly from the study but would receive a R250 travel compensation.

To ensure confidentiality and anonymity of participants, I captured all data from the survey and the CPM procedure under a participant ID and I did not use any personal identifier variables in the analyses. Moreover, only myself and my supervisors had access to the raw data and only I handled the analysis of the data. To ensure transparency of my data and analyses (without identifiers), all of my code and relevant outputs have been made available on Figshare, with links to each script provided under the respective data analysis method section for both parts of the thesis (Section 2.2.3 and 2.3.6).

2.2 Part 1: Survey

2.2.1 Participants

I invited male and female individuals of 18 years old and above, who grew up in, and currently residing in, South Africa, to participate in an online survey (Appendix 3). Information was provided to potential participants prior to starting the survey to inform them that the overall goal of the survey was to determine the association between adult attachment and pain perception (Appendix 3). To ensure a wide representation of South African individuals in the collected sample, the survey introduction and link were distributed via social media platforms (Instagram, Facebook and LinkedIn) and university emails at the University of the Witwatersrand, University of the Free State, and the University of Cape Town, all of which are in South Africa. Data collection for the survey occurred between September 2021 and April 2022. The survey was only available in English, so only individuals who could read English at a high school level would have been able to complete the survey.

2.2.2 Survey

I collected and managed the survey data using REDCap electronic data capture tools hosted at the University of the Witwatersrand (Harris et al., 2009, 2019). Data were collected from September 2021 to April 2022 and the survey consisted of customised questionnaires that assessed demographic and socio-economic factors, including age, race, sex, education and annual household income. Socioeconomic status was categorised according to each participant's reported annual household income; defined as low (ZAR 1 – ZAR 19 200), middle (ZAR 19 201 – ZAR 307 200) or high income (> ZAR 307 200) categories (Statistics South Africa, 2011). Psychosocial factors and pain-related variables were also assessed using other standardised questionnaires. As detailed below, the psychological factors assessed were adult attachment style, stress, anxiety and depression, using the Experience in Close Relationships - Relationship Structures Questionnaire (Fraley et al., 2011), and the Depression, Anxiety and Stress Scale 21 (Lovibond and Lovibond, 1995), respectively. The pain-related variables that were assessed included pain catastrophising (using the Pain Catastrophizing Scale questionnaire (Sullivan et al., 1995) and presence of chronic pain (defined as pain most days for at least the last three months (Treede et al., 2019). Participants who reported having chronic pain were also required to complete the Brief Pain Inventory – short form questionnaire (Cleeland and Ryan, 1994; Cleeland, 2009) to determine the severity of pain, location of pain, number of pain sites, and pain interference. It is worth noting, however, that there is a lack of validation of the standardised questionnaires in a South African population.

2.2.2.1 Adult attachment style

I used the Experience in Close Relationships - Relationship Structures (ECR-RS) Questionnaire to assess adult attachment style. The ECR-RS is a 9-item questionnaire with a 6-item subscale for avoidance and a 3-item subscale for anxiety, and has been previously validated in a non-clinical sample (Fraley et al., 2011). The 9-items are repeated four times, each with respect to a different relationship (a relationship with a mother/mother-like figure, father/father-like figure, romantic partner, and best friend). The questionnaire is scored on a 7-point Likert scale anchored at 1 (representing "strongly disagree") to 7 (representing "strongly agree"). The mean scores for the six avoidance subscales and three anxiety subscales for each relationship were calculated, and the mean of these scores over the four relationships provide the global dimensions for attachment anxiety and avoidance (Fraley et al., 2011). The global dimensions were then classified into adult attachment styles based on the 4-category model of attachment (Bartholomew and Horowitz, 1991). A score ≤ 4 for both attachment anxiety and attachment avoidance dimensions was classified as a "Secure" adult attachment style, while a score of > 4 for both attachment dimensions was classified as a "Fearful" adult attachment style. A score ≤ 4 for the attachment anxiety dimension but >4 for the attachment avoidance dimension was classified as a "Dismissing" adult attachment style. Lastly, a score ≤ 4 for the attachment avoidance dimension and > 4 for the attachment anxiety dimension was classified as a "Preoccupied" adult attachment style. Individuals with a Fearful, Dismissing or Preoccupied attached style were collectively classified as having an "Insecure" attachment style. Figure 1.3 shows the interactions between the dimensions and how attachment anxiety can extend to represent "belief in self", and attachment avoidance can extend to represent "belief in others" (Bartholomew and Horowitz, 1991; Mikulincer and Shaver, 2007). The reason for choosing to use the ECR-RS questionnaire instead of the more commonly used Experience in Close Relationships – Revised questionnaire is because the ECR-RS provides a way of using the attachment scores for 4 of the most common attachment figures (Doherty and Feeney, 2004) to create global attachment scores. Attachment figures tend to shift from parental figures in childhood to romantic partners, friends, family, or even psychologists/therapists in adulthood (Doherty and Feeney, 2004; Kahn and Antonucci, 1980; Sable, 2008). As such, an individual's attachment style with their parents (attachment figures developed as a child) may be completely different to attachment styles with their romantic partner or best friend (attachments developed in adulthood). The ECR-RS global attachment calculation allows for taking all the attachment styles into account, giving a more generalisable, as opposed to attachment figure-specific, attachment style.

2.2.2.2 Depression, anxiety and stress

I used the Depression, Anxiety and Stress Scale 21 (DASS-21) to measure depression, anxiety and stress (Lovibond and Lovibond, 1995). The DASS-21 has been validated in a South African non-clinical population (Dreyer et al., 2019) and has been found to be an effective measure of depression in patients with chronic pain due to the absence of questions about somatic symptoms (Taylor et al., 2005). The DASS-21 is a 21-item questionnaire with three 7-item subscales assessing depression, anxiety and stress. The questionnaire was scored on a 4-point Likert scale anchored at 0 (representing "never" applies to the individual) to 3 (representing "almost always" applies to the individual). The total score for each subscale was 21, which is then multiplied by two to get a full form score out of 42 for each subscale (Lovibond and Lovibond, 1995). The DASS-21 scores illustrate the level of depression, anxiety and stress for an individual with a score considered above normal if it is greater than 9 for depression, 7 for anxiety and 14 for stress (Lovibond and Lovibond, 1995).

2.2.2.3 Pain Catastrophising

I used the Pain Catastrophising Scale (PCS) questionnaire to measure the participant's perceived threat value of pain. Pain catastrophising, as a cognitive-emotional response, amplifies the perception of threat from pain through excessive worrying over the pain, leading individuals to anticipate greater harm or danger (Petrini and Arendt-Nielsen, 2020). As such, pain catastrophising was used as a measure of threat because it reflects the individual's heightened perception of pain and distress, indicating an increased psychological response to the perceived threat of pain. The PCS is a 13-item questionnaire assessing pain rumination, pain magnification and helplessness, and has previously been validated in a non-clinical sample (Sullivan et al., 1995). The PCS was scored on a 5-point Likert scale anchored at 0 (representing "not at all") to 4 (representing "all the time"). The highest possible score for the PCS questionnaire is 52 and indicates maximum pain catastrophising cognitions (Sullivan et al., 1995).

2.2.2.4 Chronic pain

I classified chronic pain as pain experienced most days for the last three months (Treede et al., 2019). Participants who reported having chronic pain, completed The

Brief Pain Inventory – short form (BPI-sf) questionnaire (Cleeland and Ryan, 1994), which was used to determine pain severity, location of pain, number of pain sites, and pain interference. The questions were scored on a numerical rating scale (NRS) anchored at 0 (no pain) to 10 (worst pain imaginable). A total pain severity score was calculated by finding the mean of the reported pain intensities of the participants' worst, least, average and current pain over the last week (Cleeland, 2009). Similarly, the pain interference score was calculated by finding the mean of reported interference of pain in general activity, mood, walking, work, relations with people, sleep, and enjoyment of life (Cleeland, 2009). Participants who did not have chronic pain and were women were offered the opportunity to volunteer to participate in Part 2 of the my research.

2.2.3 Data analysis

Before determining whether chronic pain was associated with attachment style, I needed to determine sufficient coverage of all four attachment styles in the survey data. Based on the prevalence of adult attachment styles in European and North American populations, where the least frequent attachment style (Preoccupied attachment style) had a prevalence ranging from 4% to 13 % (Bakermans-Kranenburg and van IJzendoorn, 2009; Coe et al., 1995), I ran a power analysis and determined that a minimum sample size of 2305 was required to answer the question of whether adult attachment style is associated with chronic pain prevalence in a general South African population with a 95% confidence level of certainty. For the sample size calculation, n = sample size, t = confidence interval (used 1.96 at a 95% confidence interval), p = estimated prevalence (used the lowest previously reported prevalence of 4%) and d = (1/5 of p) = 0.008. I used the following formula:

$$n = \frac{t^2 * p(1-p)}{d^2}$$

I closed the survey after eight months of data collection due to no new responses being recorded and the minimum sample size of 2305 fully completed surveys being met.

I only used surveys where the participants had completed the demographic questionnaire, DASS-21, PCS, ECR-RS questionnaires and answered the question on the presence of chronic pain to analyse the relationship between attachment and chronic pain prevalence. Similarly, I only used surveys where the participants had completed the demographic questionnaire, DASS-21, PCS, ECR-RS questionnaires, answered the question on the presence of chronic pain and completed the BPI-sf to analyse the relationship between attachment and chronic pain burden.

Descriptive data are reported as total number (N) and percentages (%) for categorical data, and skewed continuous data are represented as median [interquartile range (IQR)]. I used variations of generalised linear models and linear regression models for my inferential analyses. For my primary analysis (the relationship between adult attachment style and chronic pain prevalence), I ran a univariate logistic regression model for adult attachment style with chronic pain, using incidence rate ratios (IRR) to describe the relationship. Thereafter, I ran a multivariate logistic regression model to control for covariate and confounding factors for chronic pain, excluding collider variables. I also performed a subsequent multivariate mediation analysis to assess the direct effect of adult attachment style on chronic pain. For my secondary analysis (first aim, objective two) looking at the relationship between adult attachment style and the measures of the burden of chronic pain (chronic pain severity, interference and number of pain sites), I ran univariate linear regression models (adult attachment with pain severity, interference or pain sites). Subsequently, I ran multivariate linear regression models (including covariates and confounders) and multivariate mediation analyses for each measure of the burden of pain. Lastly, I performed a dropout analysis to compare the attachment styles, gender, annual household income, age, depression, anxiety and pain catastrophising between individuals who reported chronic pain but did not complete the BPI-sf and those who reported chronic pain and completed the BPI-sf. The dropout analysis was for the purpose of identifying possible reasons for lack of completion of the BPI-sf questionnaire.

Figure 2.1 illustrates the different types of variables to explain why variables were included or excluded in the multivariate models. Data were reported as odds ratios and crude estimates (95% confidence interval [CI]) for the logistic regressions, IRR and crude estimates (95% [CI]) for Poisson regressions and estimates with 95% [CI] for linear regressions. I performed all data processing and analyses in the R statistical environment (v4.2.1) (R Core Team, 2022), using the following packages: DHARMa

(Hartig, 2022), emmeans (Lenth, 2022), lme4 (Bates et al., 2015), pscl (Jackman, 2020), psych (Revelle, 2022), sjPlot (Lüdecke, 2022), tidyverse (Wickham et al., 2019) and VGAM (Yee et al., 2015). I considered a p-value of <0.05 to be statistically significant for all analyses. All data, analysis scripts and analysis script outputs are available at Figshare: 10.6084/m9.figshare.25469356.

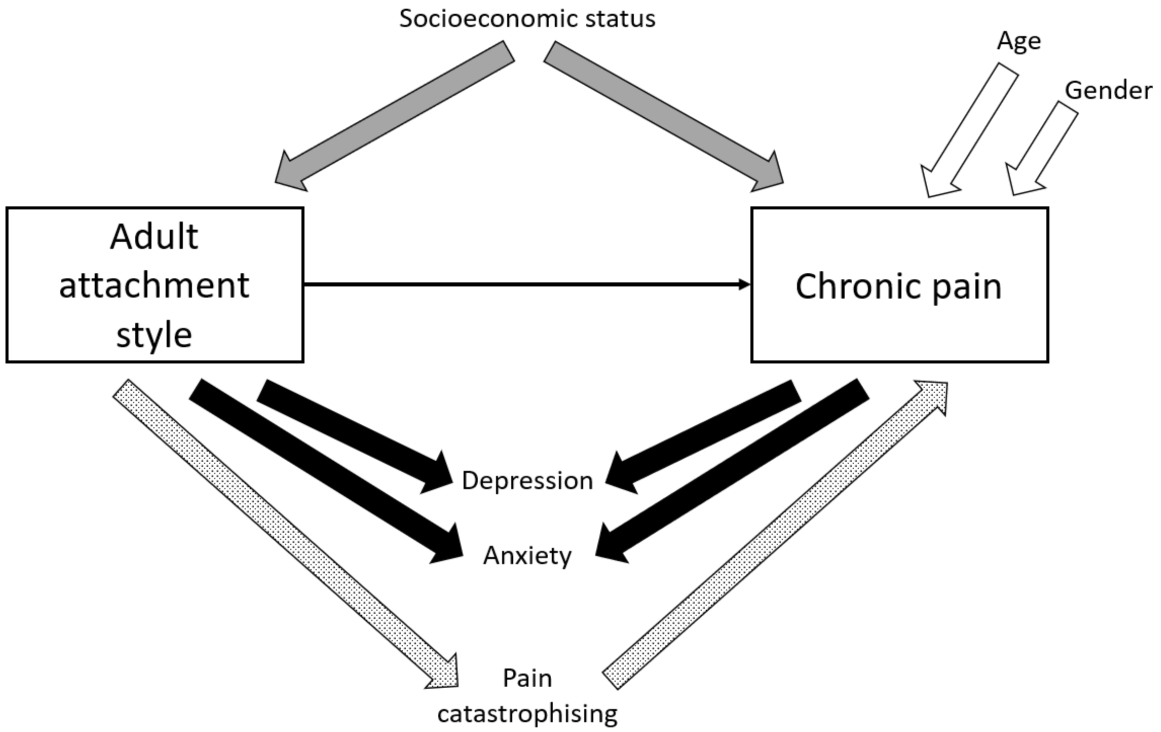

Figure 2.1: Types of variables analysed in the study, and how each of them were accounted for in the multivariate analyses. *Age and gender have been previously found to affect chronic pain (white arrows), making them* covariate *factors* (Kamerman et al., 2020)*. Socioeconomic status has been found to affect adult attachment style* (Sakman et al., 2022) *and chronic pain* (Prego-Domínguez et al., 2021) *(grey arrows), making it a* confounding *factor. To determine the total effect of the independent variable (adult attachment style) on the outcome variable (chronic pain), both confounders and covariates should be, and were, accounted for in a multivariate analysis. Both adult attachment style and chronic pain have been found to affect depression and anxiety* (Humo et al., 2019; Rajkumar, 2022; Yamauchi et al., 2022) *(black arrows), making them* collider *variables. A collider should be, and was, removed from multivariate models* (MacKinnon and Lamp, 2021)*. Lastly, adult attachment style has been found to affect pain catastrophising* (McWilliams and Holmberg, 2010)*, which in turn, has been found to affect chronic pain* (Severeijns et al., 2001) *(pattern arrow), making it a* mediating *factor. Mediators should also be excluded from a model when looking for the total effect of the independent variable on the outcome variable. However, mediators should be included when looking for a direct effect of the independent variable on the outcome variable (a mediation analysis)* (MacKinnon and

Lamp, 2021)*. As such, to look for a total effect of adult attachment style on chronic pain prevalence/burden, I excluded pain catastrophising in the multivariate model. To determine the direct effect of adult attachment style on chronic pain prevalence/burden, I ran a mediation analysis that included pain catastrophising in the multivariate model.*

2.3 Part 2: Experimental pain model

2.3.1 Participants

I invited participants who were women and had no chronic pain as determined from the data collected during the survey (Part 1) to partake in the in-person Part 2 experimental procedure. Also, I encouraged participants to invite others to participate in Part 2 of my research, to attract additional participants through word-of-mouth. All new potential participants needed to complete the survey and meet the inclusion criteria before being allowed to participate in Part 2.

I excluded male participants from Part 2 since there are known biological and psychological differences in pain between males and females (Myers et al., 2003; Wiesenfeld-Hallin, 2005). While the sex differences in experimental pain are not consistent in the literature (Racine et al., 2012), to avoid any potential sex differences confounding the findings of my research, I only included females in Part 2. Additionally, it has been found that the gender of the experimenter affects the perception of experimental pain in participants (Levine and De Simone, 1991). Moreover, matching the gender of the experimenter and the participant reduces the effect of social gender constructs on pain perception (Levine and De Simone, 1991), and since I (the experimenter) am a female, only females were invited to participate in the experimental procedure.

To partake in Part 2, I required participants to be physically healthy individuals and were excluded from the experimental investigation if they had a history of chronic pain, if they have any co-morbidities (diabetes, obesity, hypertension), as well as if they had any physical disability. Individuals with physical disabilities were excluded due to the high prevalence of co-morbidities such as hypertension, diabetes, post-traumatic stress disorder, substance use disorder, heart disease and chronic pain (Anderson et al., 2014; Rana et al., 2024; Scott et al., 2009). In addition, to minimise the possibility of psychological variables specific to experimenter manner (or relationship with the experimenter) affecting the pain perception (Andrews et al., 2011), I also excluded participants if they were current friends or family of myself, the experimenter.

The association between adult attachment style and mechanisms of endogenous pain inhibition (CPM) has not, to my knowledge, been previously investigated. To ensure unbiased data collection, the experimenter was blinded to the attachment style of the participants. Due to the low prevalence of Insecure adult attachment styles in healthy population and the fact that the attachment style could not be known by myself, the experimenter, before the CPM procedure took place, it was not possible to ensure equal size groups for each attachment style (i.e., it was not possible to ensure that the same number of individuals from each adult attachment style participated in the study). Since there was no estimate of standard deviation from past literature and the groups were different sizes, I could not run a power analysis. Previous studies looking at the association between adult attachment and experimental pain had sample sizes ranging from 30 to 95 (See Table 1.1 under Section 1.6.1 for details). As such, I stopped allowing participants to book their participation slots once 100 participants had completed the experimental procedure. Individuals who had already booked their slots prior to me reaching 100 completed participants were still allowed to participate (see booking details under Section 2.3.2). I also chose 100 participants as my stop point based on the lowest prevalence of Insecure attachment style (Fearful attachment) in individuals without chronic pain from my survey being 4%. Therefore, a sample with 100 participants should yield at least 4 participants for each attachment style, thus increasing the likelihood of all attachment styles being represented in my sample.

Data collection for Part 2 of the thesis took place between November 2022 to June 2023.

2.3.2 Overall procedure

I emailed an information sheet (Appendix 5), that described all of the experimental procedures, including what was expected of the participant and what the participant could expect from being part of the experiment, to each potential participant who met all inclusion criteria. Thereafter, I provided interested participants with a link that they could use to book their day and timeslot for participation through a scheduling platform called Calendly. When the potential participants arrived at the School of Physiology lab (where the experiment took place), I asked if they had read the information sheet and if had any questions before proceeding any further. Thereafter, I handed a laptop with an electronic consent form (Appendix 6) to read through and complete to the individuals who chose to participate. Once I obtained informed consent, participants completed an electronic questionnaire (Appendix 7) to assess current pain status and menstrual cycle information. I collected and managed the consent form and questionnaire data using REDCap electronic data capture tools hosted at the University of the Witwatersrand (Harris et al., 2009, 2019). Once all forms had been completed, the participant handed the laptop back to myself, the experimenter, to begin the experimental procedure using a CPM protocol (Lie et al., 2017). I, the experimenter, detailed the procedure of each step and made sure that the participant understood the procedures and was willing to continue. I then performed the CPM test once per participant. An overview of the procedure is summarised in Figure 2.2 to highlight where measures were taken to address each objective for Part 2 of my research.

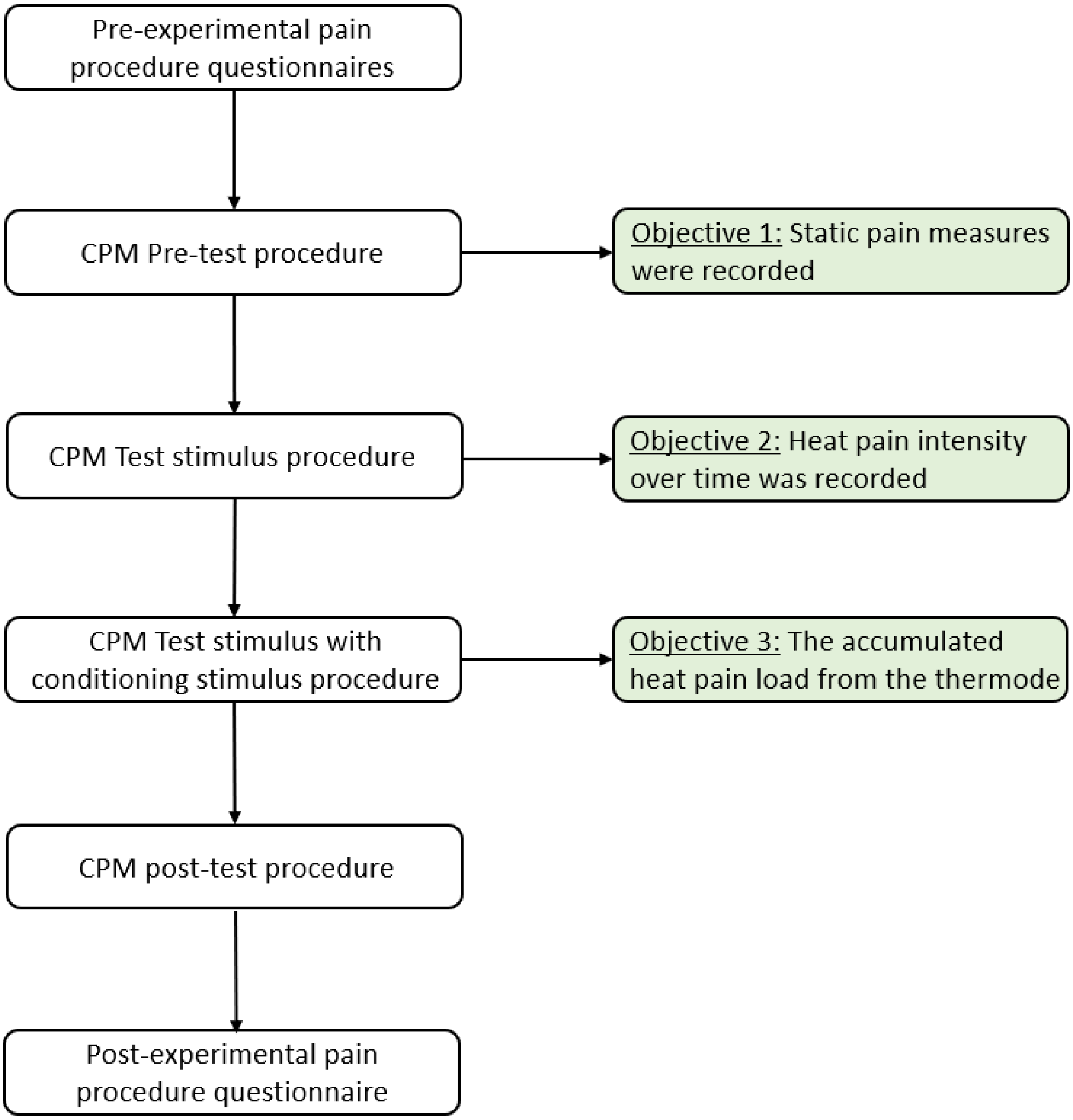

Figure 2.2: An overview of the experimental pain procedure, highlighting at what phase the measures to address each objective for Part 2 of the thesis were taken. *CPM, conditioned pain modulation.*

To control the social context, I maintained a professional (providing accurate and well-communicated information) and neutral (trying neither to be warm nor cold/distant towards participants) manner. I used a script to ensure I used the same language each time (Appendix 4). Since I collected all the data myself, I imposed a 10-minute recess between participants to collect myself, to reduce the effect of daily stressors or successes on my manner. Also, given the evidence that pain sensitivity follows the endogenous circadian rhythm (Daguet et al., 2022), I collected all data in a tight four-hour window, between 10:30 to 14:30, to minimise any circadian effects on pain sensitivity.

2.3.3 Pre-experimental pain procedure questionnaire: Current pain status and menstrual cycle information

To be included in the study, participants needed to be pain free at the time of the procedure and could not have taken any analgesic medication less than six hours prior to the procedure. To confirm this, the first questionnaire was a customised questionnaire (Appendix 7) to determine the participant's current pain status and whether they had taken pain medication in the last six hours prior to their participation. Most common over-the-counter analgesics have a maximum analgesic effect duration of 6 hours (Sobieraj et al., 2019). The questionnaire also assessed menstrual information including whether the participant was pregnant, experienced a menstrual cycle, was currently menstruating and when the date of the start of their last menstruation.

2.3.4 Experimental pain procedure

A CPM model using a tonic heat stimulus with cold pain as the conditioning stimulus was used (Lie et al., 2017).

2.3.4.1 Equipment setup

I seated participants on a comfortable chair between the testing laptop and the cold-water bath with their feet resting on a foot stool. I positioned the participants such that they were close enough to comfortably lower their arm into the water bath while seated. I placed the testing laptop in a wooden cabinet (Figure 2.3) to ensure that no testing data was visible to the participant. I only used the testing laptop to run the procedure using software Sense652 (SENSELab, Somedic Sales AB, Sweden) by connecting the SENSELab Modular Sensory Analyzer thermode machine (MSA thermal stimulator, Somedic, Sösdala, Sweden). I used a separate laptop to capture the heat thresholds and tolerances as well as all reported heat and cold pain intensities throughout the procedure. Details on the setup of the equipment are shown in Figure 2.3, with Figure 2.4 illustrating how the equipment was positioned on the participant at different stages of the CPM procedure.

Figure 2.3: The setup of the equipment used in the experimental pain procedure. *The participants sat on the red chair, with their feet on the blue stool, making it easier to rest their forearm on the thermode that was placed on their left leg for the pre-test procedure and on the right leg for the test simulus and test stimulus with conditioning stimulus procedures. I (the experimenter) sat on the green stool where I managed the temperature of the thermode on the laptop and captured the results and ratings from the experimental procedure.*

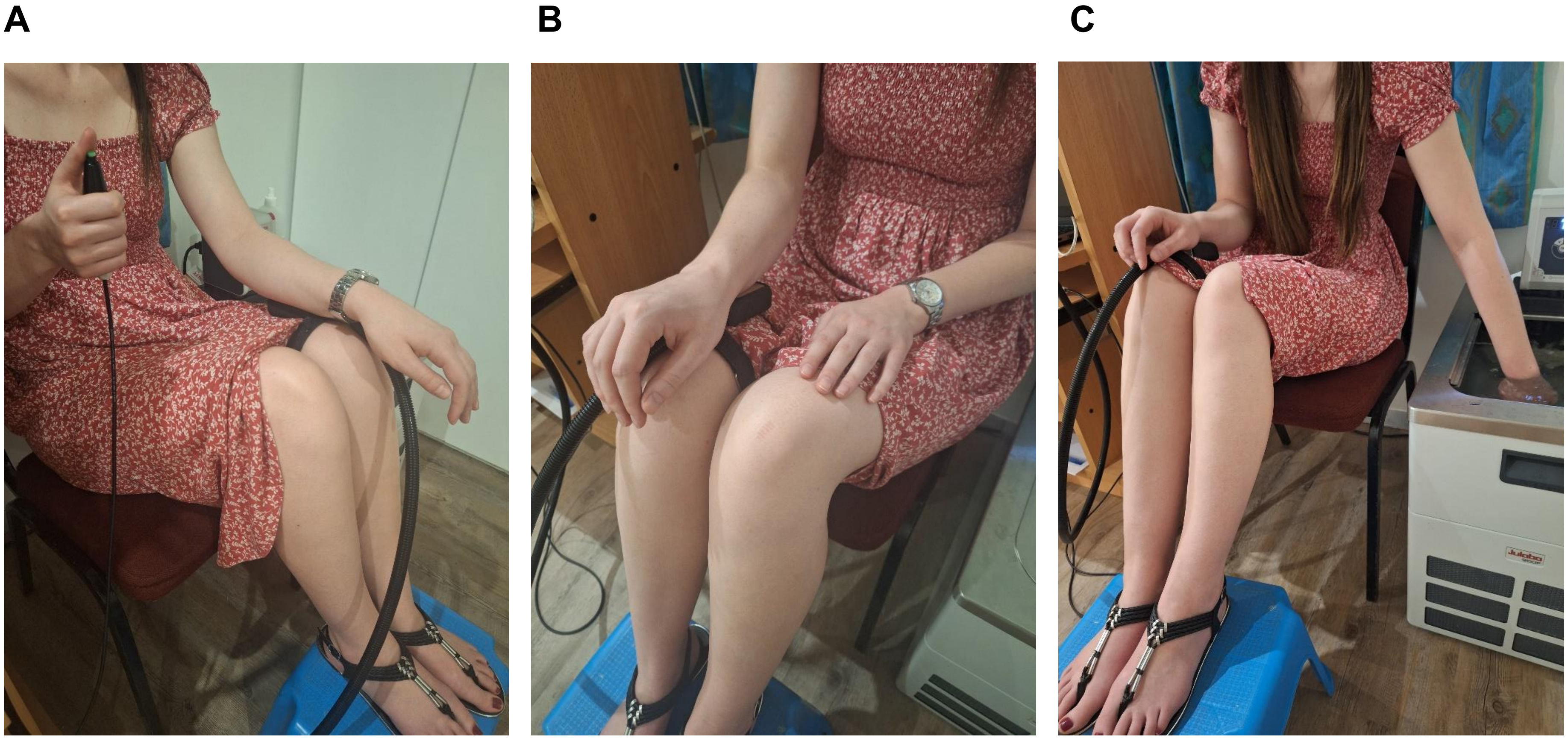

Figure 2.4: The equipment setup for the participant in the pre-test procedure (Panel A), test stimulus procedure (Panel B) and the test stimulus with conditioning stimulus procedure (Panel C).

2.3.4.2 Static measures of pain

Described in detail in Section 2.3.4.3-2.3.4.5, I recorded static measures of pain (heat pain threshold (HPT), heat pain tolerance level (HPTL) and single-point cold pain intensity). I took and recorded the HPT and HPTL measures during the pre-test procedure, detailed in Section 2.3.4.3. HPT was determined as the temperature at which the participant felt that the temperature from the thermode on the volar aspect of their left forearm changed from feeling warm to feeling painful. HPTL was determined as the temperature at which the participant could no longer stand the pain from the thermode on the volar aspect of their left forearm. I took and recorded the single-point cold pain intensity measure immediately following the conditioning stimulus procedure, detailed in Section 2.3.4.5. I asked the participants to rate the intensity of the pain (on an 11-point NRS anchored at “0, no pain” to “10, worst pain imaginable”) in their left hand from the cold water bath.

2.3.4.3 CPM Pre-test procedure

As a pre-test, I determined the participants’ test stimulus intensity by strapping a 25x50mm Peltier thermode onto the participant’s left thigh, such that the thermode plate (where the temperature will change) was facing upwards. The position of the thermode on the thigh needed to be such that the participant could comfortably rest the middle-to-distal volar aspect of their left forearm on the thermode. As such, the position of the thermode on the thigh varied slightly between participants, but all participants had their left arm positioned the same on the thermode. The thermode was initially at its baseline temperature of 32°C, while participants had their left arm resting on the thermode. First, I assessed the participants’ HPT. I told the participants when the temperature would start increasing to eliminate the effect of anticipation. I gave the participants a button to hold in their right hand and told them that the temperature of the thermode would increase gradually from 32°C to a maximum 50°C. I instructed them to push the button the moment that the temperature from the thermode changed from feeling warm to feeling painful, and recorded that temperature. I repeated the threshold procedure a total of three times, with a 10 second break between each stimulus and an average of the three was calculated and recorded as each participant’s HPT.

Next, I assessed the participants' HPTL. I performed the same procedure as described above but here I instructed participants to only push the button when the temperature from the thermode became unbearable. I told the participants when the temperature would start increasing and reminded them that the thermode would not cause any tissue damage, harm or lasting pain. I repeated the pain tolerance procedure a total of three times, with a 60 second break between stimuli and the average of the three values was calculated and recorded as HPTL. The HPT and HPTL measures were used to calculate (immediately) an estimated test stimulus temperature using the equation: ((HPTL – HPT)/2) + HPT (Lie et al., 2017). I did not use the HPT and HPTL measures any further in for the CPM procedure but analysed them for pain comparisons during data analysis.

I determined the final test stimulus temperature by assessing the temperature of the calculated estimated test temperature as well as temperatures 1°C above and below the estimated test temperature, creating three estimated test temperatures. I tested each estimated test temperature three times for 5 seconds with a 10-second interval between each test. For this procedure, I asked the participants to keep their left arm (that they previously had resting on the thermode) off the thermode while the thermode temperature was set. Once the thermode was at the required temperature, I instructed the participants to rest their left proximal volar aspect of their forearm on the thermode until they were instructed to lift it again after 5 seconds. I asked participants to rate the pain from the thermode during each 10 second break on an 11-point NRS anchored at "0, no pain" to "10, worst pain imaginable". I recorded the NRS ratings for each temperature and calculated their averages. I used the stimulus that had an average NRS rating closest to 6/10 as the final test stimulus. If the NRS rating for all three temperatures did not fall within 4-9, I tested additional estimated temperatures until the NRS rating fell within these parameters. I recorded the final test temperature used for the participant's test stimulus. The CPM pre-test procedure is summarised in Figure 2.5 for clarity.

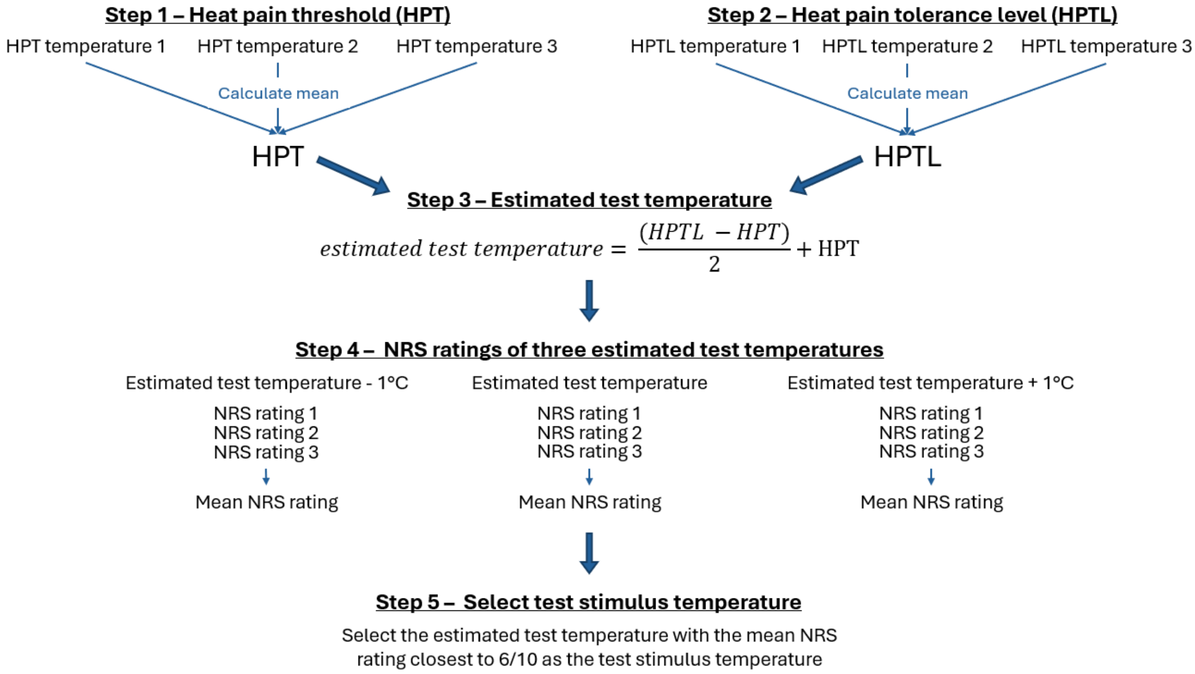

Figure 2.5: An overview of the conditioned pain modulation pre-test procedure process. *NRS, Numerical rating scale.*

2.3.4.4 CPM Test stimulus procedure

For the test stimulus procedure, I placed the same 25x50mm Peltier thermode on the right leg of the participant, face up, such that the participant could comfortably rest the distal volar aspect of their right arm on the thermode. Since the thermode was already set to the test temperature, I asked the participant not to touch the mental plate of the thermode. I then instructed the participant to rest the right volar aspect of their forearm on the thermode for 120 seconds. The temperature of the thermode remained at the test temperature for the duration of the procedure. As soon as the participant placed their arm on the thermode, I started a stopwatch. Every 10 seconds I asked the participant to give a rating for the pain intensity from the thermode by saying "thermode". The rating was given using the 11-point NRS and I recorded each rating. I calculated and recorded the mean NRS ratings for every 30 second interval during the duration of the test stimulus (0–30, 31–60, 61–90, and 91–120 seconds) as well as for the entire 120 second period (Lie et al., 2017).

2.3.4.5 CPM Test stimulus with conditioning stimulus procedure

Five minutes after concluding the test stimulus procedure described above, I asked participants to immerse their left hand, up to the wrist, in a water bath (ThermoFisher Scientific 19L Circulating Water Bath, Massachusetts, United States of America) of circulating 7°C water (painful cold stimulus). I reminded all participants that the cold water would not cause any tissue damage, harm or lasting pain. I asked participants to keep their hand relaxed with slightly spread fingers to allow the water contact with their whole hand. This cold water bath stimulus was the conditioning stimulus. At the same time, I also asked participants to place the distal volar aspect of their right forearm back on the thermode (the test stimulus), just as they had done for the test stimulus procedure. I asked participants to keep both their right arm on the thermode and their left hand in the water for the full duration of 120 seconds, although I made it clear that they may choose to withdraw from either stimulus if they felt the need to. The moment that both stimuli were in position, I repeated the test stimulus procedure, as described above, in parallel with the cold water conditioning stimulus. I asked participants to rate the pain intensity from the thermode every 10 seconds when I said "thermode". I recorded the test stimulus pain intensity ratings and then averaged them in the same manner as for the test stimulus procedure. These thermode rating obtained from this procedure will be referred to as the test stimulus pain intensity ratings during the conditioning procedure.

2.3.4.6 CPM Post-test procedure

After the hand was withdrawn from the water at 120 seconds, the conditioning stimulus average pain intensity (the pain intensity in response to the cold water) was rated by the participants using the 11-point NRS (Lie et al., 2017) and I recorded their rating. The intensity of the cold pain stimulus was only rated once, following the completion (or partial completion) of the CPM procedure. Part-way into data collection (after 44 participants had already completed their CPM procedure), I added an additional question following their rating of the cold water pain intensity. The new question asked participants to rate (using the 11-point NRS) what they expected the pain intensity from the cold water to be. I added the question following the observation that some participants seemed more apprehensive about putting their hands in the cold water than others, and expectation is known to influence pain perception (Bjørkedal and

Flaten, 2012; Fields, 2018) and differ between adult attachment styles (Mikulincer and Shaver, 2007).

2.3.5 Post-experimental pain procedure questionnaire

I then asked participants to fill in a customised electronic qualitative questionnaire on the laptop (Appendix 8). The questionnaire assessed aspects of the participant's overall experience of the experiment. Part of this post-experiment questionnaire was the main goal of this assessment: how they rated the manner of the experimenter (the participants were able to choose from three options: "Friendly", "Neutral/Professional", "Aloof"). This question served as a check to determine if the participants perceived my (the experimenter's) manner as neutral/professional, as was the intention. I encouraged participants to complete this entire questionnaire with honesty, and not with what they believed were supposed to be the "correct" answers. I added further questions after data collection had already started (after 44 participants had already completed the procedure); these were added for the purpose of exploring responses and providing possible reasons for any associations that may have arisen in the analysis of the data. In particular, I added questions to assess whether the heat or cold stimuli were perceived as "threatening", together with open-ended questions asking the participants to describe their experience of both the hot and cold stimuli (Appendix 8).

2.3.6 Data analysis

I analysed data from all participants for the models run between adult attachment style and psychological variables, experimenter manner, single-point pain measures (heat pain threshold, tolerance and cold pain intensity) and pain intensity of the test stimulus (both the average pain intensity as well as the pain intensity over time for the cumulative pain load). I only analysed data from participants who had completed the full CPM procedure (kept their hand submerged in the cold water bath for the full duration of 120 seconds) in the primary analysis models between adult attachment style and the CPM effect (defined efficacy of endogenous pain inhibition, taken as the difference between the test stimulus pain intensity rating prior to conditioning and the test stimulus pain intensity ratings during conditioning, as described in more detail below).

Prior to assessing the CPM effect, I ran univariate analyses by performing Welch Two Sample t-tests to compare the heat pain thresholds and tolerances and average intensity over 120 seconds between the Secure and Insecure adult attachment styles. Since the CPM effect is calculated as the difference between the test stimulus thermode pain intensity before and during the conditioning stimulus procedure, I determined a difference in the perception of the pain intensities before investigating the efficacy of the descending pain inhibiting pathways by looking at the CPM effect. I determined the average pain intensity rating from the thermode test stimulus prior to the conditioning procedure by calculating the mean of each individual rating, which was given every 10 seconds for 120 seconds. I ran a linear regression model between pain intensity prior to conditioning and time to determine an overall cumulative pain load of the test stimulus alone. Thereafter, I included adult attachment style in the model and ran a multiple linear regression model to determine the difference in cumulative pain load (as determined by the area under the curve (AUC)) of the test stimulus alone between the two broad groups of adult attachment styles.

To determine whether the CPM effect was successfully induced in the participants, I ran a linear regression model between the test stimulus pain intensity prior to the conditioning procedure and the test stimulus pain intensity during the conditioning procedure. Thereafter, I added adult attachment style to the model and performed a multiple linear regression to compare the change in heat pain intensity from the test stimulus prior to and during the conditioning procedure between the two attachment styles. Moreover, I determined the average pain intensity rating from the thermode test stimulus during the conditioning procedure by calculating the mean of each individual thermode rating, which was given every 10 seconds for 120 seconds in the conditioning procedure. Following a predefined protocol, I defined the absolute CPM effect as the difference in pain ratings from the thermode test stimulus pain ratings before the conditioning procedure compared to the thermode test stimulus pain ratings during the conditioning procedure (Absolute CPM effect = pain rating from thermode test stimulus prior to the conditioning procedure – pain rating from thermode test stimulus during the conditioning procedure) (Lie et al., 2017). I further calculated the CPM effect as a percent change of the thermode test stimulus rating prior to conditioning (CPM effect percentage = (absolute CPM effect/thermode test-stimulus rating prior to conditioning) x 100) (Lie et al., 2017). The calculation of CPM effect in this manner has been recommended by pain researchers (Yarnitsky et al., 2015). I used the CPM percentage for analyses and ran a Welch Two Sample t-test to determine the difference in CPM effect for the two adult attachment styles. I also ran a linear regression model between the thermode test stimulus pain intensity ratings every 10 seconds prior to conditioning and the thermode test stimulus pain intensity ratings every 10 seconds during the conditioning procedure. I used this linear regression to determine whether there was an overall pain inhibition in the participants and whether the adult attachment interacted with the relationship between the thermode test stimulus pain intensity ratings prior to and during the conditioning procedure.

As part of exploratory analyses, I performed sensitivity analyses using a multiple imputation model where missing CPM effect data were adjusted for in two different ways: (1) The last reported thermode test stimulus pain intensity from during the conditioning phase was carried forward for all remaining 10-second unreported intervals and (2) the average thermode test stimulus pain intensity rating from the test stimulus phase (prior to conditioning) over the 120 seconds was carried forward in the conditioning phase for the 23 participants who did not complete the CPM procedure.

I reported descriptive data as total number (N) and percentages (%) for categorical data and median [IQR] for skewed continuous data. For analysis between the two-category adult attachment style and categorical variables (including completion of the CPM procedure and experimental manner), I ran a Chi Square test. I reported results from the Chi Share models as X^2(df) = Chi Square statistic, p = p-value). I ran a Welch two-sample t test for all analyses between the two-category adult attachment styles and continuous variables (including depression, anxiety, heat pain threshold and tolerance temperatures, pain intensity ratings and the CPM effect percentage). I reported the results from the t test as t(df) = t-statistic, p = p-value, accompanied by a mean difference [95%CI]. I reported linear regression model results as Estimate [95%CI].

I performed all data processing and analyses in the R statistical environment (v4.2.1) (R Core Team, 2022), using the following packages: DHARMa (Hartig, 2022), emmeans (Lenth, 2022), lme4 (Bates et al., 2015), pscl (Jackman, 2020), psych (Revelle, 2022), sjPlot (Lüdecke, 2022), tidyverse (Wickham et al., 2019) and VGAM (Yee et al., 2015). I considered a p-value of <0.05 to be statistically significant for all analyses. All data, analysis scripts and analysis script outputs are available at Figshare: 10.6084/m9.figshare.25479397.

CHAPTER 3

PART 1 – RESULTS AND DISCUSSION

3.1 Results

Overall, there were 3356 survey entries from the data collection period (September 2021 to April 2022), of which 2371 individuals completed the entire survey and were included in the primary statistical analyses. The age range of the participants was 18 to 80 years old with a median [IQR] of 23 [20-28] years. At least secondary education had been completed by 99% (2362 of 2371) of the participants, and 79% (1877 of 2371) of the participants had an annual household income of greater than ZAR19 200,00 (considered as middle and high income households (Statistics South Africa, 2011)). The prevalence of chronic pain was 27% (635 of 2371) in our sample. More details of my survey cohort are described in Table 3.1.

Table 3.1: A summary of the demographic data and adult attachment style proportions in the 2371 survey respondents.

Characteristic	**Final sample N (%)**
Gender	
Men	596 (25)
Women	1747 (74)
Other	28 (1)
South African Province	
Eastern Cape	53 (2)
Free State	382 (16)
Gauteng	1277 (54)
Kwa-Zulu Natal	113 (5)
Limpopo	43 (2)
Mpumalanga	37 (1)
Northern Cape	14 (1)
North West	28 (1)
Western Cape	424 (18)
Race/Ethnicity	
Asian	18 (1)
Black	956 (40)
Indian	161 (7)
Mixed race	119 (5)
White	1062 (45)
Other	55 (2)
Annual household income	
No income	115 (5)
Low income	379 (16)
Middle income	1030 (43)
High income	847 (36)
Adult attachment style*	
Secure	1 824 (77)
Dismissing	246 (10)
Preoccupied	172 (7)
Fearful	129 (6)

** Adult attachment style was assessed using the Experience in Close Relationships – Relationship Structures (ECR-RS) Questionnaire* (Fraley et al., 2011).

Univariate models were run between chronic pain prevalence and various demographic and psychosocial variables (including adult attachment style). These univariate associations are summarised in Table 3.2. Greater prevalence of chronic pain was significantly associated with gender (being a woman), adult attachment styles (having an Insecure attachment), household income (having a lower income), and higher depression, anxiety and pain catastrophising. The reference variables for the univariate logistic regression models were “Men” (for gender), “Secure” (for the adult attachment style) and “No income” (for annual household income).

Table 3.2: Factors associating with the presence of chronic pain in the 2371 survey respondents.

	No chronic pain (N (%))	Chronic pain (N (%))	Odds ratio (95%CI)	p-value
Total	1736 (73.22)	635 (26.78)	-	-
Gender				
Men	***457 (76.68)***	***139 (23.32)***	-	-
Women	1259 (72.07)	488 (27.93)	1.27 (1.03-1.59)*	**0.028***
Other	20 (71.43)	8 (28.57)	1.32 (0.53-2.95)*	0.524*
AAS[a]	129			
Secure	***1400 (76.75)***	***424 (23.25)***	-	-
Dismissing	170 (69.11)	76 (30.89)	1.48 (1.10-1.97)**	**0.009****
Preoccupied	100 (58.14)	72 (41.86)	2.38 (1.72-3.27)**	**<0.001****
Fearful	66 (51.16)	63 (48.84)	3.15 (2.19-4.53)**	**<0.001****
AHI	847			
No income	***74 (64.35)***	***41 (35.65)***	-	-
Low income	241 (63.59)	138 (36.41)	1.03 (0.67-1.61)***	0.882***
Middle income	742 (72.04)	288 (27.96)	0.70 (0.47-1.06)***	0.085***
High income	679 (80.17)	168 (19.83)	0.45 (0.30-0.68)***	**<0.001*****
	No chronic pain (median [IQR])	**Chronic pain (median [IQR])**	**Incidence rate ratio (95%CI)**	**p-value**
Age	23 [20-28]	23 [21-31]	1.06 (1.03-1.10)	**0.001**
Depression[b]	10 [4-20]	18 [8-28]	1.43 (1.34-1.52)	**<0.001**
Anxiety[b]	8 [4-16]	16 [8-24]	1.59 (1.49-1.69)	**<0.001**
Pain catastrophising[c]	14 [6-24]	24 [13-36]	1.56 (1.47-1.65)	**<0.001**

The bolded, italicized lines show the reference variable for each analysis.
** Association when compared to men*
*** Association when compared to the Secure adult attachment style*
**** Association when compared to the no income group*
AAS, Adult attachment style
AHI, Annual household income
Bolded = p<0.05
[a] *Adult attachment style was assessed using the Experience in Close Relationships – Relationship Structures (ECR-RS) Questionnaire* (Fraley et al., 2011).
[b] *Depression and anxiety were assessed using the Depression, Anxiety and Stress Scale 21 (DASS-21)* (Lovibond and Lovibond, 1995).
[c] *Pain catastrophising was assessed using the Pain Catastrophising Scale (PCS)* (Sullivan et al., 1995).

3.1.1 Primary analysis: Is there an association between adult attachment style and chronic pain prevalence?

To determine the association between adult attachment style and chronic pain prevalence, two multiple logistic regression models were run. Table 3.3 shows the results of these regressions with Secure as the reference attachment style. The first model investigates a total effect of adult attachment on chronic pain. The second model ("Direct effect") is a mediation analysis showing the mediating effect of pain catastrophising on the relationship between adult attachment style and chronic pain prevalence, including confounders (annual household income), covariates (age and gender), but excluding the colliders (depression and anxiety).

Table 3.3: Multivariate analyses showing the total and direct effect of adult attachment style on chronic pain in the total sample (N = 2371).

	Total effect*		**Direct effect****	
AAS	*Adjusted odds ratio (95%CI)*	*p-value*	*Adjusted odds ratio (95%CI)*	*p-value*
Secure	-	-	-	-
Dismissing	1.38 (1.02-1.85)	**0.037**	1.10 (0.80-1.51)	0.545
Preoccupied	2.26 (1.62-3.13)	**<0.001**	1.51 (1.06-2.14)	**0.021**
Fearful	2.95 (2.03-4.29)	**<0.001**	1.94 (1.31-2.89)	**0.001**

AAS, Adult attachment style relative to secure attachment style
** Multivariate model including confounders (annual household income) and covariates (age and gender), but excluding colliders (depression and anxiety) and mediators (pain catastrophising)*
*** Multivariate model including confounders (annuals household income), covariates (age and gender) and mediators (pain catastrophising), but excluding colliders (depression and anxiety)*
Bolded = p<0.05

There was a total effect of each adult attachment style on chronic pain prevalence. Pain catastrophising mediated the relationship between Dismissing attachment and chronic pain prevalence, but both Preoccupied and Fearful attachment were directly associated with chronic pain prevalence.

3.1.2 Secondary analysis: Is there an association between adult attachment and the burden of chronic pain?

The secondary analysis explored the burden of pain (through number of pain sites, pain severity and pain interference) for the four different attachment styles using the results of the Brief Pain Inventory. Two hundred and eight individuals were classified as having chronic pain but did not complete the BPI-sf. Thus, only 427 individuals (those with chronic pain who completed the BPI-sf questionnaire) were included in the secondary analysis. A dropout analysis showed the following associations with those that had dropped out: these individuals were more likely to be male (compared to female) (Odds ratio [CI], 0.64 [0.43 – 0.94], p=0.024) with significantly lower depression (Odds ratio [CI], 0.97 [0.96 – 0.99], p<0.001), anxiety (Odds ratio [CI], 0.96 [0.94 – 0.97], p<0.001) and pain catastrophising (Odds ratio [CI], 0.99 [0.98 – 1.00], p=0.037).

The pain severity and pain interference scores for the adult attachment styles are summarised in Figure 3.1. Two separate univariate linear regression models were run for adult attachment with pain severity score and pain interference score. Compared to the Secure attachment style, the Dismissing (Estimate [95%CI] = 0.48 [0.00-0.96], p-value = 0.049) and Fearful (Estimate [95%CI] = 0.88 [0.36-1.40], p-value = 0.001) attachment styles significantly predicted higher pain severity scores. Pain interference scores were significantly higher in Dismissing (Estimate [95%CI] = 0.70 [0.04-1.37], p-value = 0.038), Preoccupied (Estimate [95%CI] = 0.93 [0.23-1.63], p-value = 0.010) and Fearful (Estimate [95%CI] = 1.31 [0.59-2.03], p-value<0.001) attachment styles when compared to Secure attachment. Multivariate analyses were run to determine the total and direct effect of adult attachment style on pain severity and pain interference score. The Fearful adult attachment style was associated with a total effect of higher pain severity score when compared to the Secure attachment (Estimate [95%CI] = 0.78 [0.26-1.30], p = 0.004). Pain catastrophising mediated the relationship between attachment style and pain severity, resulting in no direct associations between adult attachment style and pain severity score. There was also a total effect of all three insecure attachment styles being associated with worse pain interference scores when compared to the Secure attachment style (Dismissing: Estimate [95%CI] = 0.73 [0.06-1.41], p = 0.032; Preoccupied: Estimate [95%CI] = 0.88 [0.17-1.58], p = 0.015; Fearful: Estimate [95%CI] = 1.17 [0.44-1.90], p = 0.002). Pain catastrophising also mediated the relationship between adult attachment and pain interference, resulting in no direct associations.

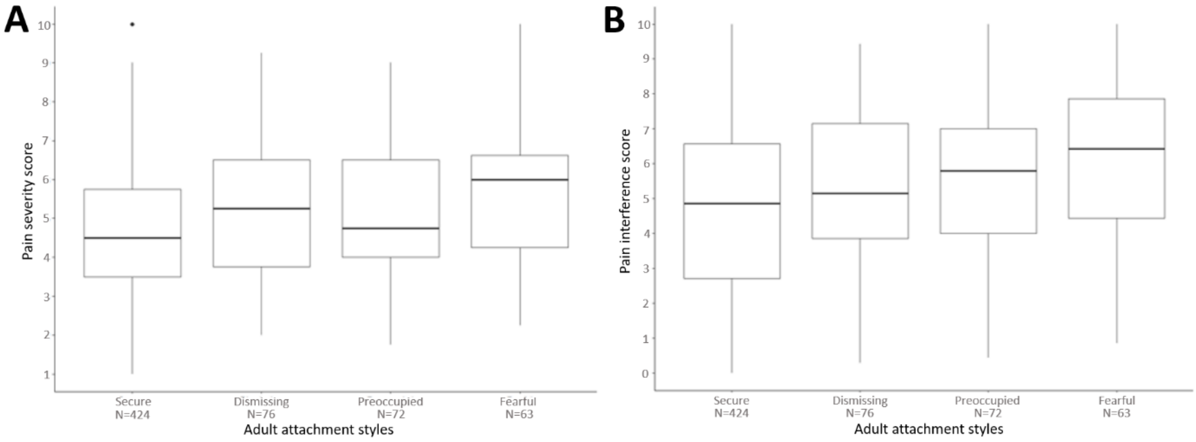

Figure 3.1: Pain severity score (Panel A) and Pain interference score (Panel B) in the last week for the four different adult attachment styles in individuals with chronic pain who completed the Brief Pain inventory – short form (BPI-sf) (N=427).

All three insecure adult attachment styles were associated with increased pain catastrophising when compared to Secure attachment (Dismissing: IRR [95%CI] = 1.25 [1.08-1.44], p = 0.002; Preoccupied: IRR [95%CI] = 1.28 [1.10-1.48], p = 0.001; Fearful: IRR [95%CI] = 1.50 [1.30-1.73], p < 0.001). Moreover, higher pain catastrophising was associated with higher pain severity scores (Estimate [95%CI] = 0.04 [0.02-0.05], p < 0.001) and higher pain interference scores (Estimate [95%CI] = 0.07 [0.05-0.08], p < 0.001). For clarity on the mediation between adult attachment and pain severity and interference through pain catastrophising, these results are summarised in Figure 3.2.

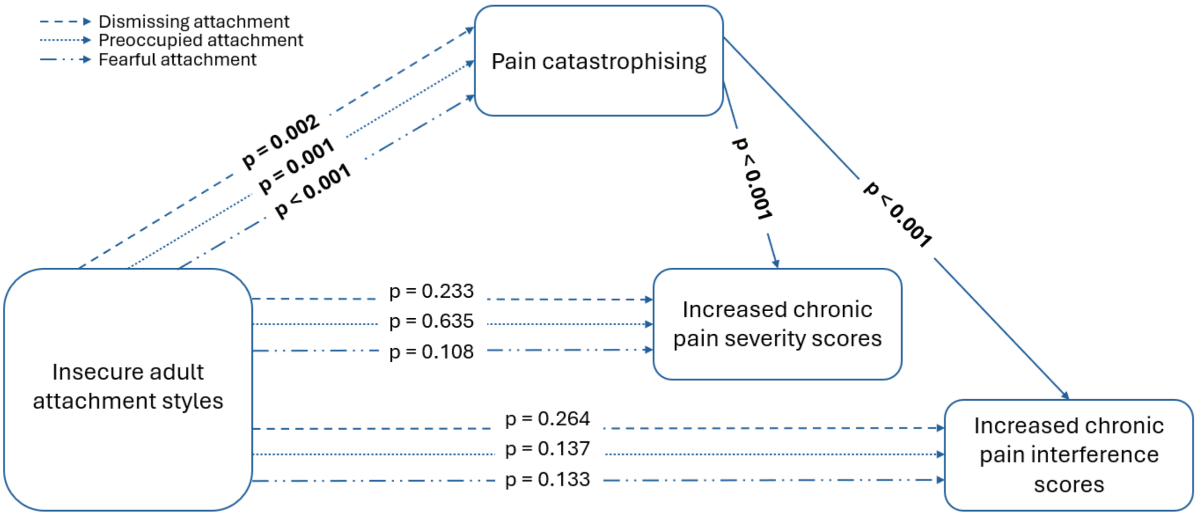

Figure 3.2: The mediation pathway between the insecure adult attachment and increased chronic pain severity and interference scores through pain catastrophising. *Bolded p-values shows statistically significant associations.*

With regards to number of painful body sites in individuals reporting chronic pain, a univariate analysis showed that individuals with a Preoccupied attachment had 1.32 times more pain sites (95% CI: 1.10-1.56, p=0.002) and individuals with Fearful attachment had 1.30 times more pain sites (95% CI: 1.09-1.55, p=0.003) than individuals with Secure attachment. Individuals with Dismissing attachment did not have a difference in the number of pain sites compared to the Securely attached individuals. After running multivariate analyses for the number of pain sites across the various attachment styles, there was a total effect whereby the Preoccupied and Fearful adult attachment style were associated with more pain sites compared to the Secure attachment style (Preoccupied: Estimate [95%CI] = 1.92 [0.71-3.13], p = 0.002; Fearful: Estimate [95%CI] = 1.78 [0.54-3.02], p = 0.005). After running a mediation analysis that accounted for pain catastrophising, there was a direct effect whereby there was an increased number of pain sites for both the Preoccupied (Estimate [95%CI] = 1.68 [0.46-2.90], p = 0.007) and Fearful (Estimate [95%CI] = 1.36 [0.08-2.64], p = 0.037) attachment styles when compared to Secure attachment.

3.1.3 Dimension data

In Chapter 4, I assess differences in the threat perception and the CPM effect for the two adult attachment dimensions (attachment anxiety/belief in others and attachment voidance/belief in self) in the female experimental cohort. I then discuss the dimension score ranges for the females who participated in the experimental study when compared to the score ranges of the pain-free females in the general survey population. As such, here I present the dimension data for the pain-free females from the general survey population for comparison purposes. I also present the dimension data of those pain-free females from the survey who volunteered to participate in the experimental phase of my research (Part 2).

For all the pain-free female survey participants, the attachment anxiety dimension scores ranged from 1.0 – 7.0 (median [IQR] = 2.3 [1.6-3.2]) and the attachment avoidance scores ranged from 1.0 – 6.1 (median [IQR] = 2.9 [2.2-3.5]). For the pain-free female survey participants who volunteered to participate in Part 2 of my thesis, the attachment anxiety dimension scores ranged from 1.0 – 6.5 (median [IQR] = 2.5 [1.8-3.3]) and the attachment avoidance scores ranged from 1.0 – 6.1 (median [IQR] = 3.0 [2.2-3.6]). For comparison of these data to the dimension data from the females who participated in Part 2 of my research, see Figure 4.9, Section 4.2.2.

3.2 Discussion

I conducted a survey of over 2000 individuals to determine associations between adult attachment style and prevalence of chronic pain. In my young, well-educated and primarily female (74%) cohort, with a predominantly middle-to-high socioeconomic status, I found that Insecure attachment styles were associated with an increased prevalence of chronic pain. Both Preoccupied and Fearful styles were directly associated with prevalence of chronic pain, and of note, the prevalence of chronic pain was more than double in individuals with a Fearful attachment style compared to securely attached individuals. The relationship between adult attachment style and two out of the three measures of burden of pain (pain intensity and interference) was mediated by pain catastrophising in those with chronic pain, although Preoccupied and Fearful adult attachment styles were directly associated with more pain sites than those with Secure attachment. Still, taking all three measures of the burden of chronic pain together, adult attachment style was not directly associated with the burden of chronic pain, although the effect of pain catastrophising as a mediator emphasises the impact of psychological factors on the relationship between adult attachment and chronic pain. My data contribute to the emerging idea that a relationship exists between attachment style and chronic pain. To my knowledge, this is the first report that attachment style in a general population is associated with chronic pain prevalence, and notably, pain catastrophising mediates the relationship between attachment and the burden of chronic pain.

Chronic pain prevalence is typically low in young people. For example the prevalence of chronic pain in a young (18 – 25 years) population in the United Kingdom has been reported to be as low as 14% compared to the general prevalence that ranged from 35% - 51% over various studies (Fayaz et al., 2016). A study conducted on a United States of America cohort also found a lower prevalence of chronic pain (7.5%) in young adults (18 – 24 years) compared to the general population (21%). Previously published data in a national sample of South Africans have demonstrated that 13% of 24-34 year olds have chronic pain (Kamerman et al., 2020). In that same study (Kamerman et al., 2020), the prevalence of chronic pain in women was 20% across all age groups, which is noteworthy since pain is more prevalent in women than in men (Racine et al., 2012), and 74% of my cohort was female, possibly explaining the high chronic pain prevalence in my sample. In my study, the prevalence of chronic pain was 23% in the securely attached individuals, but 39% in individuals with Insecure attachment styles. Indeed, specifically within the insecurely attached individuals, those with a Fearful attachment had a 49% prevalence of chronic pain. What is remarkable is that this association with chronic pain, and these high prevalence rates of chronic pain were evident in a rather young cohort, with an average age in the early twenties (median age 23 years; IQR 20-28). In addition to most of my sample being female, the high chronic pain prevalence found in my research may be due to individuals with chronic pain being more motivated or willing to answer a survey investigating pain perception than pain-free individuals.

The association with Insecure attachment and chronic pain makes sense with overlapping neurocircuitry between physical and social pain (Eisenberger et al., 2003, 2006) and pain and expectations of social safety or threat (Eisenberger et al., 2011). Essentially, there is evidence that when one perceives an environment and/or stimulus as threatening, the intensity of pain is increased (Karos et al., 2020; Vlaeyen et al., 2009; Wang et al., 2016). Furthermore, there are associations between Insecure attachment styles and factors associated with pain including poorer mental health (Andersen, 2012; Ciechanowski et al., 2003; Kowal et al., 2015), greater number of sleep disruptions and greater levels of Inflammation (Adams and McWilliams, 2015; Gouin et al., 2009; Jaremka et al., 2013) all of which impact the perception of pain (Babiloni et al., 2020; Edwards et al., 2016). Indeed, my study found that all three Insecure adult attachment styles had significantly higher depression, anxiety and pain catastrophising when compared to individuals with a Secure attachment style. It is important to acknowledge that the high levels of depression and anxiety in my sample may have been due to, or at least exacerbated by, the COVID-19 pandemic (Bäuerle et al., 2020; Wu et al., 2021). Whilst there is evidence suggesting that an association between having chronic pain and Insecure attachment style make sense, studies exploring this association, and explicitly looking at potential mechanisms, are lacking.

One of the issues with attachment and pain literature to-date is the heterogeneity of study designs, including the reporting of attachment using Secure vs. Insecure attachment *styles*, using only the two attachment *dimensions*, or the four-category model, as I have done here. Whilst using the two dimensions (attachment anxiety and attachment avoidance) may have more power (Fraley et al., 2015), it loses the nuance of the overlap of both scales, for example, having both high attachment anxiety (low belief in self) and high attachment avoidance (low belief in others). Based on my results, I hypothesise that there may be an additive effect of having high attachment anxiety *and* avoidance, that is, a Fearful attachment style, compared to just one high dimension, as is the case for Preoccupied and Dismissing styles, since the prevalence of chronic pain in individuals with the Fearful attachment style was over 10% higher than the average chronic pain prevalence for individuals with Preoccupied and Dismissing attachment. This hypothesis requires further investigation. Perhaps future studies could investigate chronic pain prevalence in other general populations for the four adult attachment styles to determine if a similar trend is seen and if individuals with a Fearful attachment style are potentially even more at risk of developing chronic pain than individuals with Dismissing or Preoccupied attachment.

Recent work suggests that attachment style is modifiable (Fraley, 2019; Groh et al., 2014) and so even if an individual develops an Insecure attachment during childhood, a Secure attachment may be earned later in life through close, supportive relationships or psychological therapy (Olufowote et al., 2020; Saunders et al., 2011). On the other hand, there is some evidence from a 20-year longitudinal study of 50 individuals, that stressful life events later in life may lead to the *loss* of a Secure attachment style obtained in infancy (Waters et al., 2000). However, at this stage many questions regarding attachment remain unclear, including whether chronic pain may also act as one of those stressful life events that leads to loss of Secure attachment (and all its associated benefits, including improved emotional regulation and decreased physiological stress (Lewczuk et al., 2021; Palitsky et al., 2013; Pietromonaco and Powers, 2015)). That being said, the possibility of chronic pain causing a shift from Insecure to Secure attachment would make sense given that poor quality or strained relationships contribute to the reduced quality of life in patients with chronic pain (Kowal et al., 2015). Additionally, there are functional and structural changes in corticolimbic brain regions (including the prefrontal cortex, ACC, PAG, nucleus accumbens and amygdala (Figure 1.5A)) of individuals with chronic pain (Yang and Chang, 2019). These changes may result in higher depression, anxiety and anger (Yang and Chang, 2019), which could further place strain on interpersonal relationships. The somewhat opposing cause-effect question also remains unclear. In other words, in addition to the 'potential loss of a secure attachment due to pain' idea above, if one develops an Insecure attachment style from childhood interpersonal relationships, does that predispose one to the development of chronic pain, due to having unsatisfying social support networks, and hence not seeking care for acute problems (Mikail et al., 1994)? Longitudinal studies are required to answer such questions, which have important implications on treatment options, response to treatment, progression of disease, and overall quality of life in patients with chronic pain. Indeed, preliminary evidence suggests that individuals with Insecure attachments have lower adherence rates to pain management programmes and poorer psychological outcomes following pain management programmes (Andersen, 2012; Ciechanowski et al., 2003, 2001; Kowal et al., 2015). These data suggest that profiling the attachment of patients, and a better understanding of the different responses to management programmes according to attachment security, may path the way forward to personalised treatment options with more favourable clinical outcomes. Future studies could investigate the incidence of chronic pain in an at-risk population (e.g. post-operative patients) to determine if adult attachment style is associated with the incidence of chronic pain (i.e. is adult attachment style associated with the rate at which new chronic pain cases are reported?). Additionally, future studies could assess adult attachment styles over time in individuals with chronic pain to determine whether attachment styles change with increased time living with chronic pain or with worsened chronic pain burden over time. As such, future studies could determine possible causality, which could have implications for the prevention and management of pain going forward (e.g. determining at what stages psychosocial support could be added in the care pathway and to whom these psychosocial strategies could be focused on).

I found a statistically significant total difference in pain intensity, and particularly pain interference, between attachment styles, which was then mediated by pain catastrophising. Moreover, in a cohort similarly-sized to mine, with chronic widespread pain, Insecure attachment styles associated with greater number of pain sites when compared to the Secure attachment style (Davies et al., 2009). I found a similar association where a higher number of pain sites was directly associated with Preoccupied and Fearful attachment styles. While a direct association between attachment and number of pain sites was found from my analyses, pain catastrophising mediated the relationship between adult attachment and the two other measures of the burden of pain (pain severity and interference). As such, the impact of pain catastrophising as a mediator in the relationship between adult attachment and the burden of chronic pain highlights the importance of psychological factors in the perception and progression of chronic pain. The increased psychological vulnerability in Insecure, compared to Secure, adult attachment styles has also been noted in other studies (Andersen, 2012; Ciechanowski et al., 2003; Kowal et al., 2015). Importantly, pain catastrophising is a negative cognition that results in the amplification of the threat value of pain due to the constant worrying over the expectation of the pain intensity or severity (Petrini and Arendt-Nielsen, 2020). As such, the amplification of threat may be a mechanism through which pain catastrophising mediates the relationship between adult attachment and burden of chronic pain. Individuals with Secure attachment do not exhibit a hypervigilance to threat (like individuals with a low belief in self), but rather trust in their own ability to cope with the pain (Mikail et al., 1994; Mikulincer and Shaver, 2007). Moreover, Secure individuals have a sense of trust in others, such that they know they will be supported when they need help (unlike in individuals with a low belief in others) (Mikail et al., 1994; Mikulincer and Shaver, 2007). Therefore, a secure adult attachment style may protect against developing pain catastrophising by not being hypersensitive to threats and being confident in oneself and others for threat resolution. Therefore, , the association between the Insecure adult attachment styles and higher chronic pain burden could be hypothesised to be mediated by perceived threat or perceived ability to deal with the threat, which, taken one step further, suggests threat appraisal as an important factor and possible mechanism in the progression to chronic pain.

3.2.1 Limitations, strengths, and future directions

There are limitations to my study, as well as strengths, that should be acknowledged. My study was conducted in 2021 during the COVID-19 pandemic, and there is evidence of increased levels of depression and anxiety, gathered from German and Chinese populations, compared to pre-pandemic levels (Bäuerle et al., 2020; Wu et al., 2021). As such, the nature of my cohort may have been affected by the pandemic. I also recruited a convenience sample, that is, a sample of individuals responding to my social media or email advert to complete a survey on attachment style and pain. Moreover, the information page preceding the survey explained that the intention of the survey was to investigate factors that affect pain perception (Appendix 3), which may have made the survey more appealing to complete if individuals had chronic pain, possibly explaining the high chronic pain prevalence from the survey. The cohort is therefore unlikely to be truly representative of the national population. This is further supported by the fact that respondents were 75% female, 45% white, 99% had completed at least secondary education, all were able to read and write English and had access to a device and data with which to respond. This sex, education, race and socioeconomic profile is also not representative of the South African population (Statistics South Africa, 2011) as it showed that my sample was biased towards educated, white females from a middle to high socioeconomic background. These biases highlight inequities found in higher education and access to electronic devices in South Africa. However, it does make my data more generalisable to developed countries in the global north. The proportions of attachment styles may, therefore, not be representative of the general South African population. Also, participants were required to select an option for their household income, however this information may not have been known by the participant and may have skewed the annual household income data. Additionally, I used the ECR-RS questionnaire to assess adult attachment style. While this questionnaire was chosen due to its ability to obtain a more generalised attachment style, it has not been validated in a South African population, which is a limitation in my research.

Another limitation was that 33% (208/635) of the individuals with chronic pain did not complete the Brief Pain Inventory and so their pain intensity and interference data were missing. The dropout analysis indicated that there were 208 individuals with chronic pain who did not complete the Brief Pain Inventory questionnaire and that these individuals were more likely to be male. The reasons for this are unclear. Moreover, the sample of individuals with chronic pain from the survey was biased towards female participants and high levels of depression, anxiety and pain catastrophising. Both biases were expected since chronic pain is more common in females (Kamerman et al., 2020) and is associated with depression, anxiety and pain catastrophising (Lerman et al., 2015; Petrini and Arendt-Nielsen, 2020). The bias towards pain catastrophising, however, does not detract from the results of the secondary analysis, but rather places emphasis on the poor psychological health in individuals with chronic pain and insecure adult attachment styles.

Some important strengths of my survey study should be noted too. My study is the only cohort to recruit a general population and assess the association between adult attachment style and chronic pain prevalence. Moreover, my study was one of the largest cohorts investigating any kind of association between adult attachment style and chronic pain (2371 participants) with only one other study having a larger cohort (2509 participants recruited from three general practices) (Davies et al., 2009). Importantly, I was the first to assess the association between chronic pain prevalence and adult attachment style, rather than assessing the prevalence of each adult attachment style in individuals who already have chronic pain, as has previously been done (Davies et al., 2009). Previous studies have assessed associations between adult attachment styles and the burden of chronic pain, chronic pain coping strategies and/or the success of chronic pain management programmes pain (Andersen, 2012; Kowal et al., 2015; Meredith et al., 2007). These studies made use of cohorts that consisted only of individuals with chronic pain, with sample sizes ranging from 60 to 635 participants (Andersen, 2012; Andersen et al., 2018; Belot et al., 2021; Costa-

Martins et al., 2014; Kowal et al., 2015; Meredith et al., 2006b, 2007; Nasika et al., 2023; Nyland et al., 2022). The association between Insecure adult attachment styles and increased chronic pain prevalence, as found in my study, highlights Insecure attachment styles as a possible vulnerability for individuals to develop chronic pain, providing a possible avenue for further research.

3.2.2 Conclusion

In this analysis of attachment style and chronic pain in a young and primarily female cohort with a high socioeconomic status, not only did I find an association between Insecure adult attachment styles and greater prevalence of chronic pain, but chronic pain prevalence was more than double in individuals with a Fearful attachment style compared to those with a Secure attachment style. Moreover, pain catastrophising was found to mediate the association between adult attachment style and chronic pain burden, emphasising the importance of psychological factors and threat appraisals in the progression of chronic pain. I believe my results highlight the need to repeat the study not only in a more nationally representative sample, but also globally. Furthermore, longitudinal studies are required to map attachment security and incidence and outcomes of chronic pain, to determine the possible vulnerability that individuals with an Insecure adult attachment style have in developing chronic pain.

CHAPTER 4

PART 2 – RESULTS AND DISCUSSION

4.1 Results

Following the completion of the survey (N = 2371 males and females), female respondents without chronic pain who provided their email addresses and were willing to travel to the University of the Witwatersrand to participate in the experimental phase of my research, were invited to volunteer as participants in this subsequent experimental procedure aimed at investigating the relationship between attachment style and static (pain threshold, tolerance and intensity) and dynamic measures (pain intensity over time and CPM) of pain.

The process of recruitment and exclusion for Part 2 is summarised in Figure 4.1. A total of 103 participants were included in the analyses of the pain heat pain threshold, tolerance and test stimulus pain intensity data from the CPM procedure. Only 80 participants completed the entire CPM procedure (kept their hand in the cold water bath for the full duration of 120 seconds) and were included in all primary analyses of the CPM effect.

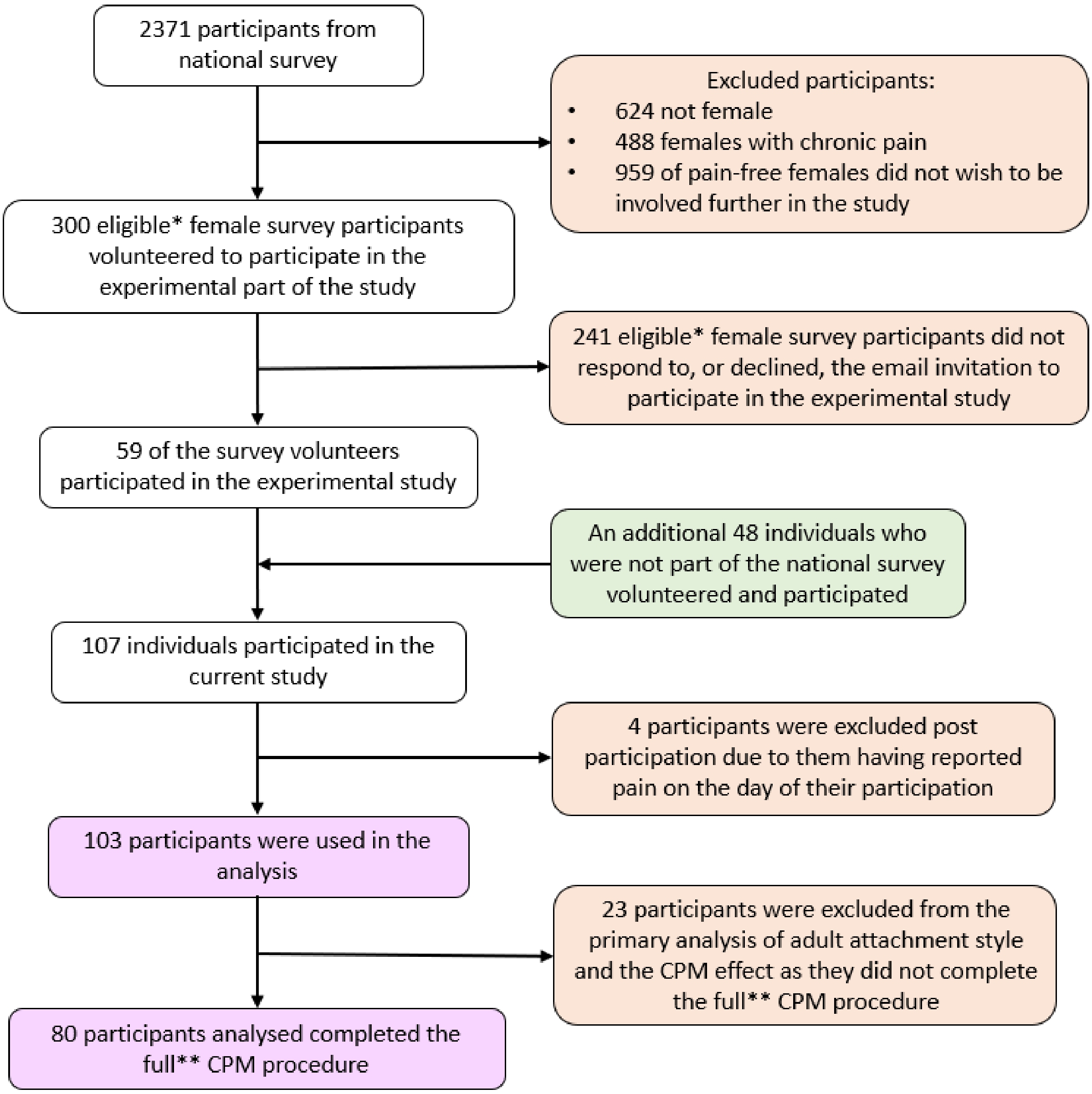

Figure 4.1: An outline of the process and numbers of volunteers, details of screening exclusion, the final number of participants in the study, and those participants included in the analyses. *CPM = Conditioned Pain modulation*

** To be eligible for participation in the study, volunteers needed to be female, 18 years old or above and not have chronic pain.*

*** Only data from participants who had completed the CPM procedure (kept their hand in the conditioning cold water bath pain stimulus for the full 120 seconds) were included in the primary analysis between adult attachment style and the CPM effect.*

The age of the participants ranged from 18 to 44 years, with a median [IQR] of 21 [20-23] years. All participants included in the analyses (N = 103) had, at least, completed secondary education, with 44% (45 of 103) of the participants having completed their undergraduate university degree. The annual household income was greater than

ZAR19 200,00 (middle and high income households (Statistics South Africa, 2011)) for 73% (75/103). More details of the sample are described in Table 4.1 including the proportion of attachment styles of participants, as determined using the Experience in Close Relationships - Relationship Structures (ECR-RS) Questionnaire (Fraley et al., 2011).

Table 4.1: Demographic frequency data and adult attachment style proportions in the 103 female participants for the conditioned pain modulation procedure.

Characteristic	**Final sample N (%)**
Race/Ethnicity	
Asian	2 (2)
Black	61 (59)
Indian	12 (12)
Mixed race	4 (4)
White	23 (22)
Other	1 (1)
Annual household income	
No income (ZAR 0,00)	4 (4)
Low income (ZAR 1,00 – ZAR 19 200,00)	24 (23)
Middle income (ZAR 19 201,00 – ZAR 307 200,00)	46 (45)
High income (ZAR 19 201,00 – ZAR 307 200,00)	29 (28)
Adult attachment style*	
Secure	73 (71)
Dismissing	14 (13)
Preoccupied	6 (6)
Fearful	10 (10)

**Adult attachment style was assessed using the Experience in Close Relationships - Relationship Structures (ECR-RS) Questionnaire* (Fraley et al., 2011)*.*
ZAR, South African Rand

Initial analyses were performed with participants split into the two broader categories of attachment style: Secure (73/103 (71%)) and Insecure, in which Dismissing, Preoccupied and Fearful styles were combined (30/103 (29%)). If statistical differences between Secure and Insecure attachment styles were detected for pain threshold, tolerance, test pain stimulus intensity, cold pain stimulus intensity and the CPM effect, additional analyses using all four attachment style categories would have been performed.

Before assessing the relationship between the two attachment styles and the measures (static and dynamic) of pain, any other differences between the Secure and Insecure participants were investigated. I investigated whether there was a difference in the number of individuals who completed the CPM procedure between the Secure and Insecure participants. To complete the CPM procedure, the participants were required to keep their hand in the cold-water bath for the full 120 seconds. The CPM procedure was completed by 78% (80 of 103) of the participants. There was no difference in the number of individuals able to complete the CPM procedure between the Secure (58/73 (79%)) and the Insecure (22/30 (73%)) attachment styles ($X^2(1) = 0.459$, $p = 0.498$).

Next, to account for experimenter manner on pain perception (Daniali and Flaten, 2019), the study was designed (I used words from a standardised script, Appendix 4) with the intention that I remained professional and neutral (see methods section 2.3.2.), and this was assessed in a post-experiment questionnaire. The results showed that 81% (83 of 103) of the participants rated my (the experimenter) manner as “Neutral/Professional”, while the remaining 19% (20 of 103) rated my manner as “Friendly”. There was no difference in the number or individuals who rated my manner as “Neutral/Professional” between the Secure (60 of 73; hence 82%) and the Insecure (23 of 30; hence 77%) attachment styles ($X^2(1) = 0.415$, $p = 0.520$).

Lastly, the differences in psychological variables of depression, anxiety and pain catastrophising between the Secure and Insecure attachment styles were investigated; these results are summarised in Table 4.2. After running a series of Welch Two Sample t-tests, the Insecure attachment style had a significantly greater levels of depression ($t(51) = 3.37$, $p = 0.001$), anxiety ($t(44) = 3.49$, $p = 0.001$) and pain catastrophising (t(47) = 3.35, p = 0.002) when compared to the Secure attachment style.

Table 4.2: Differences in psychological variables between Secure (N = 73) and Insecure (N = 30) attachment styles.

Psychological variable	Secure attachment style Median [IQR]	Insecure attachment style Median [IQR]	Mean score difference [95%CI]
Depression	6.0 [2.0-14.0]	18.0 [8.0-22.0]	8.03 [3.24-12.82]*
Anxiety	6.0 [4.0-14.0]	18.0 [6.5-21.5]	6.94 [2.93-10.96]*
Pain catastrophising	14.0 [6-21]	21.5 [14.2-32]	8.27 [3.31-13.23]*

95%CI, 95% Confidence interval
IQR, interquartile range
**, p-value < 0.05*
Depression and anxiety were assessed using the Depression, Anxiety and Stress Scale 21 (DASS-21) (Lovibond and Lovibond, 1995)*; Pain catastrophising was assessed using the Pain Catastrophizing Scale (PCS) questionnaire* (Sullivan et al., 1995)

Of the additional questions added to the post-experimental pain procedure questionnaire part-way into the data collection (after 44 of 103) two questions asked whether the participants perceived the heat and cold pain stimuli as "threatening". Overall, 22% (13 of 59) of the participants who answered this question perceived the heat pain stimulus from the thermode to be threatening, while 76% (45 of 59) of the participants perceived the cold pain from the water bath as threatening. There was no difference in threat perception between the two adult attachment styles for the heat pain (Secure: 20% (9 of 45), Insecure: 29% (4/14), $X^2(1) = 0.46$, $p = 0.499$) or cold pain (Secure: 80% (36 of 45), Insecure: 64% (9/14), $X^2(1) = 1.46$, $p = 0.227$).

4.1.1 Primary analysis: Is there a difference in the static and dynamic measures of pain between the Secure and Insecure attachment styles?

4.1.1.1 Static measures of pain (threshold, tolerance and single-point intensity)

There was no difference in the reported pain threshold temperature ($t(54) = -0.45$, $p = 0.654$, mean difference [95%CI] = -0.30°C [-1.64 – 1.04]) or tolerance temperature ($t(47) = -1.16$, $p = 0.250$, mean difference [95%CI] = -0.43 °C [-1.18 – 0.31]) between the Secure and Insecure attachment styles (Figure 4.2).

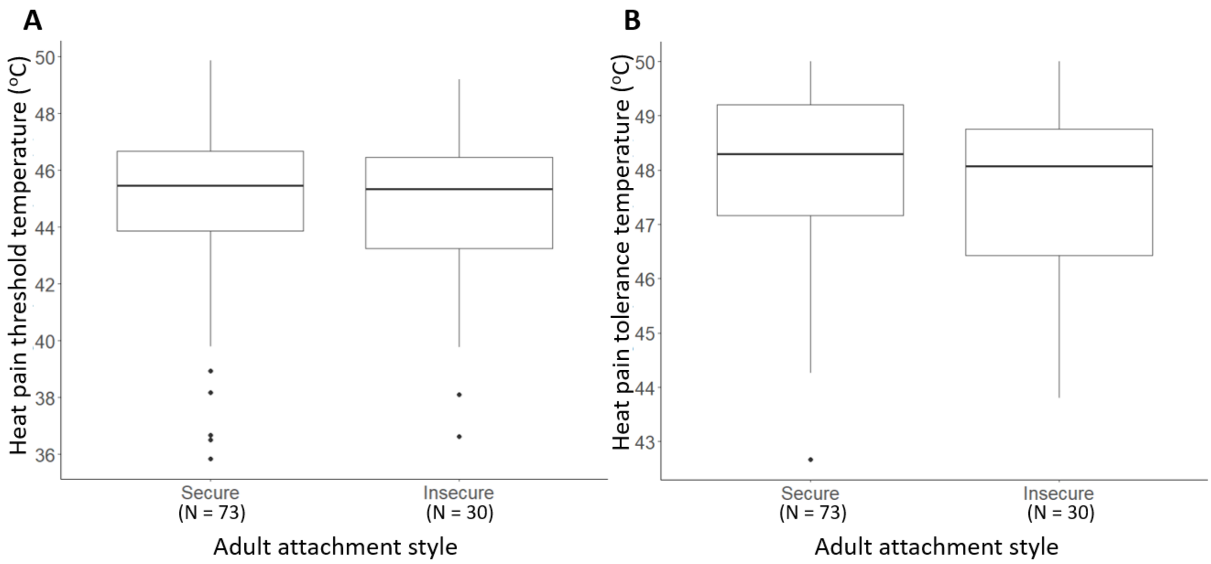

Figure 4.2: The heat pain threshold (Panel A) and tolerance (Panel B) temperatures for the two adult attachment style categories (N=103). *The heat pain threshold and tolerance temperatures were determined in the pre-test phase of the conditioned pain modulation procedure by finding the mean temperature from three consecutive heat pain threshold and heat pain tolerance tests. The box and whisker plots represent the median and IQR for the heat pain threshold and tolerance temperatures. The dots in the figure represent outliers in the data.*

There was no difference in the reported single-point intensity of the cold pain stimulus between the two adult attachment categories ($t(40) = -1.09$, $p = 0.280$, mean difference [95%CI] = -0.38 [-1.07 – 0.32]) (Figure 4.3A). There was also no association between the expected cold pain rating and the actual cold pain rating for the 59 participants (57%) who answered the expected cold pain question (Estimate [95%CI] = -0.08 [-0.25 – 0.09], $p = 0.336$). Moreover, there was no difference in the expected cold pain intensity between the 62% (45/73) of Secure and 47% (14/30) of Insecure participants who were asked this expected cold pain question ($t(22) = 1.33$, $p = 0.198$, mean difference [95%CI] = 0.70 [-0.39 – 1.79]) (Figure 4.3B).

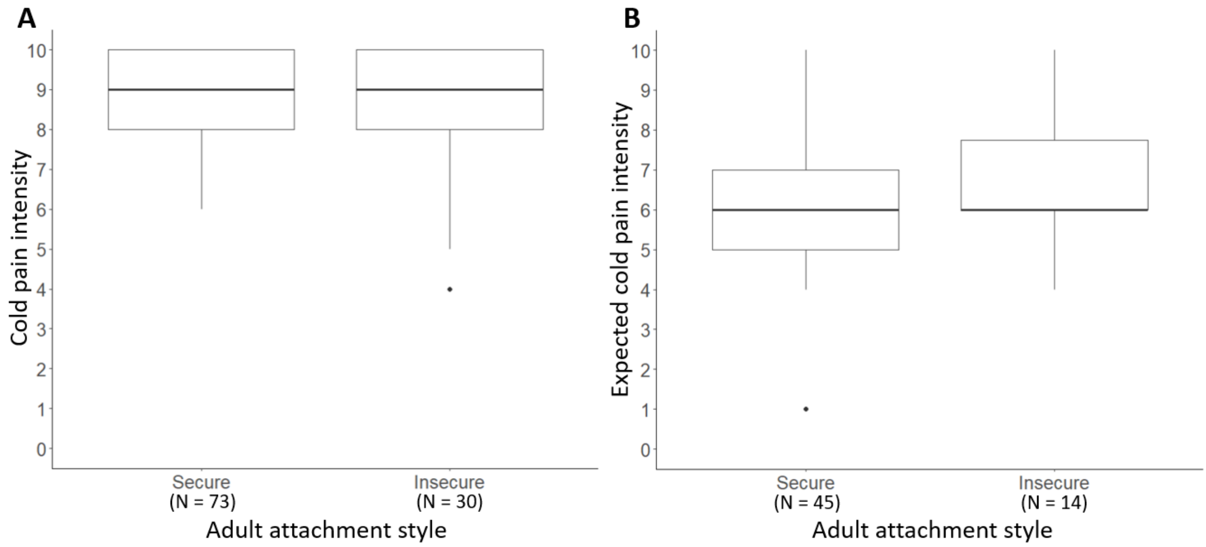

Figure 4.3: The actual cold pain intensities (N=103) (Panel A) and expected cold pain intensities (N=59) (Panel B) for the two adult attachment style categories. *The box and whisker plots represent the median and IQR for the cold pain and expected cold pain intensities.*

4.1.1.2 Dynamic measures of pain (intensity over time and conditioned pain modulation)

Before looking at the relationship between adult attachment style and the CPM effect (a way of assessing endogenous analgesia), any possible relationship between the two-category adult attachment style (Secure and Insecure) and the perception of the test stimulus pain intensity needed to be determined.

First, to determine if there was a change in the test stimulus intensity over time, a univariate linear regression model was run, showing that the reported test stimulus pain intensity increases over time (Estimate [95%CI] = 0.01 [0.00-0.01], p-value < 0.001). A total cumulative pain load over the two minutes (as determined by calculating the AUC) was calculated to be 737 rating.seconds. After running a multiple linear model to account for adult attachment style, there was no significant difference in the reported test stimulus pain intensity over time (Estimate [95%CI] = -0.11 [-0.34-0.11], p-value = 0.330), with both attachment styles having similar cumulative pain loads (Secure: AUC = 741 rating.seconds, Insecure: AUC = 727 rating.seconds). Figure 4.4 shows the relationship between reported pain intensity rating over time for the Secure and Insecure attachment style.

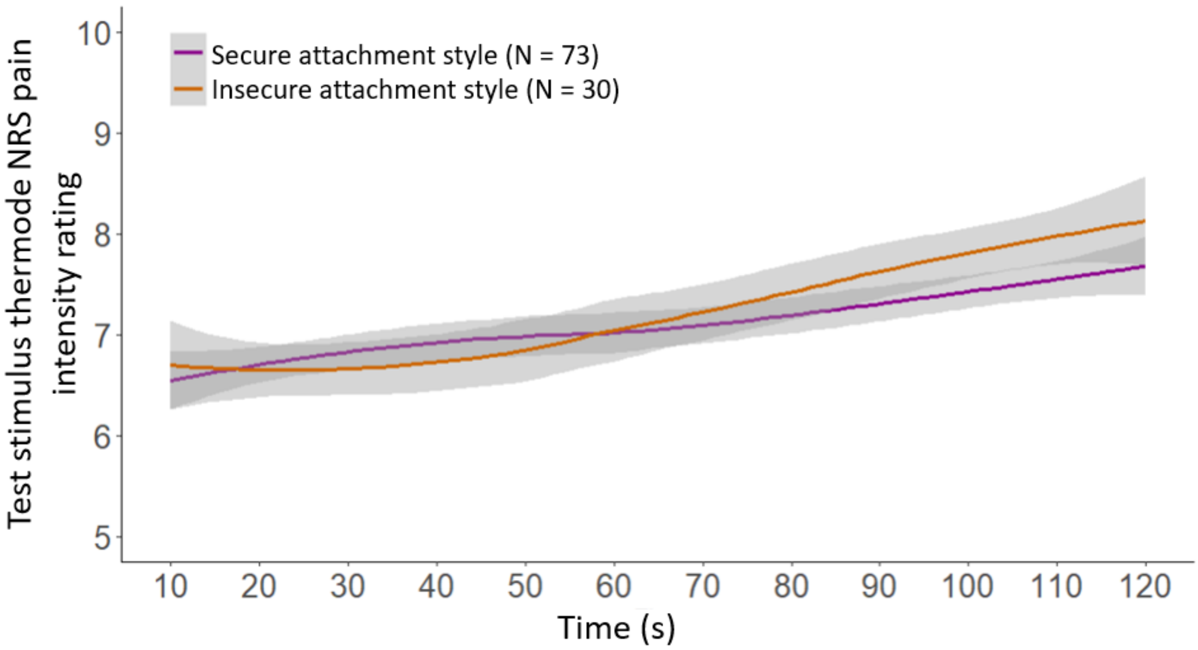

Figure 4.4: The test stimulus thermode pain intensity ratings over two minutes for the Secure and Insecure adult attachment styles. *The graph shows the fitted regression lines for each attachment style together with a grey border on each line representing the 95% confidence interval. NRS, numerical rating scale.*

Moreover, a Welch Two Sample t-test model showed no association in the average test stimulus pain intensity (calculated as a mean from the reported pain intensities from the thermode prior to conditioning every 10 seconds for 120 seconds) between the Secure and Insecure adult attachment styles ($t(50) = -0.31$, $p = 0.755$, mean difference [95%CI] = -0.11 [-0.84 – 0.61]) (Figure 4.5). In other words, the perception of the test stimulus pain intensity did not differ between the Secure and Insecure attachment style.

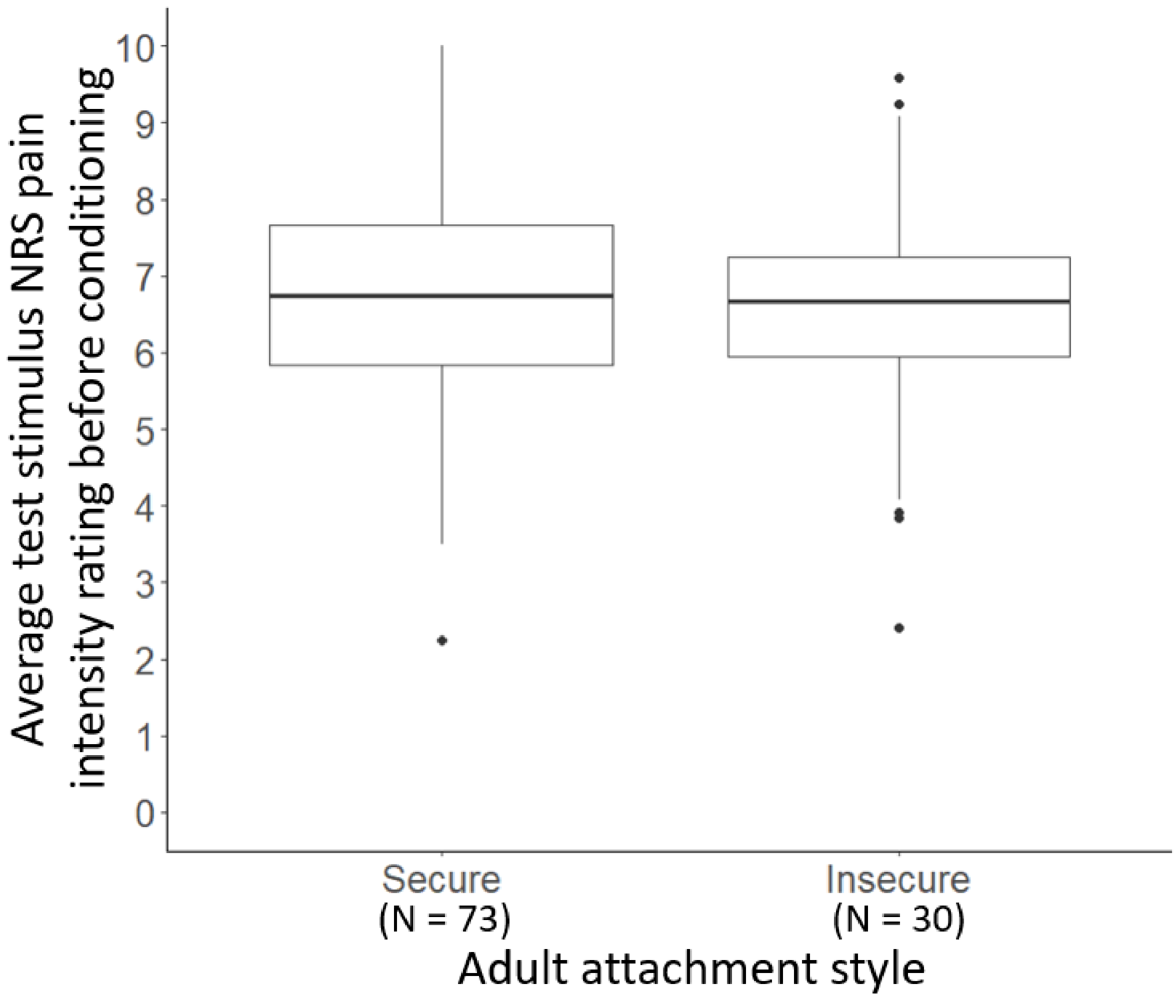

Figure 4.5: The average test stimulus pain intensity rating from the thermode prior to the conditioning procedure (measured using the Numerical Rating Scale, NRS) for the two overall adult attachment style categories (N=103). *The average test stimulus pain intensity rating prior to conditioning was calculated by finding the mean for each test stimulus rating prior to conditioning over the 120 second test stimulus prior to conditioning phase. The box and whisker plot represents the median and IQR of the average test stimulus pain intensity ratings. The dots in the figure represent outliers in the data.*

A second Welch Two Sample t-test model showed no association in the average test stimulus pain intensity during conditioning (calculated as a mean from the reported pain intensities from the thermode during conditioning every 10 seconds for 120 seconds) between the Secure and Insecure adult attachment styles ($t(37) = -0.43$, $p = 0.671$, mean difference [95%CI] = -0.23 [-1.34 – 0.87]) (Figure 4.6). Although the average pain intensity for the thermode test stimulus both before and during the conditioning procedure does not differ between the two adult attachment styles, it is still beneficial to look at the CPM effect % to determine whether the participants experienced a pain inhibitory effect.

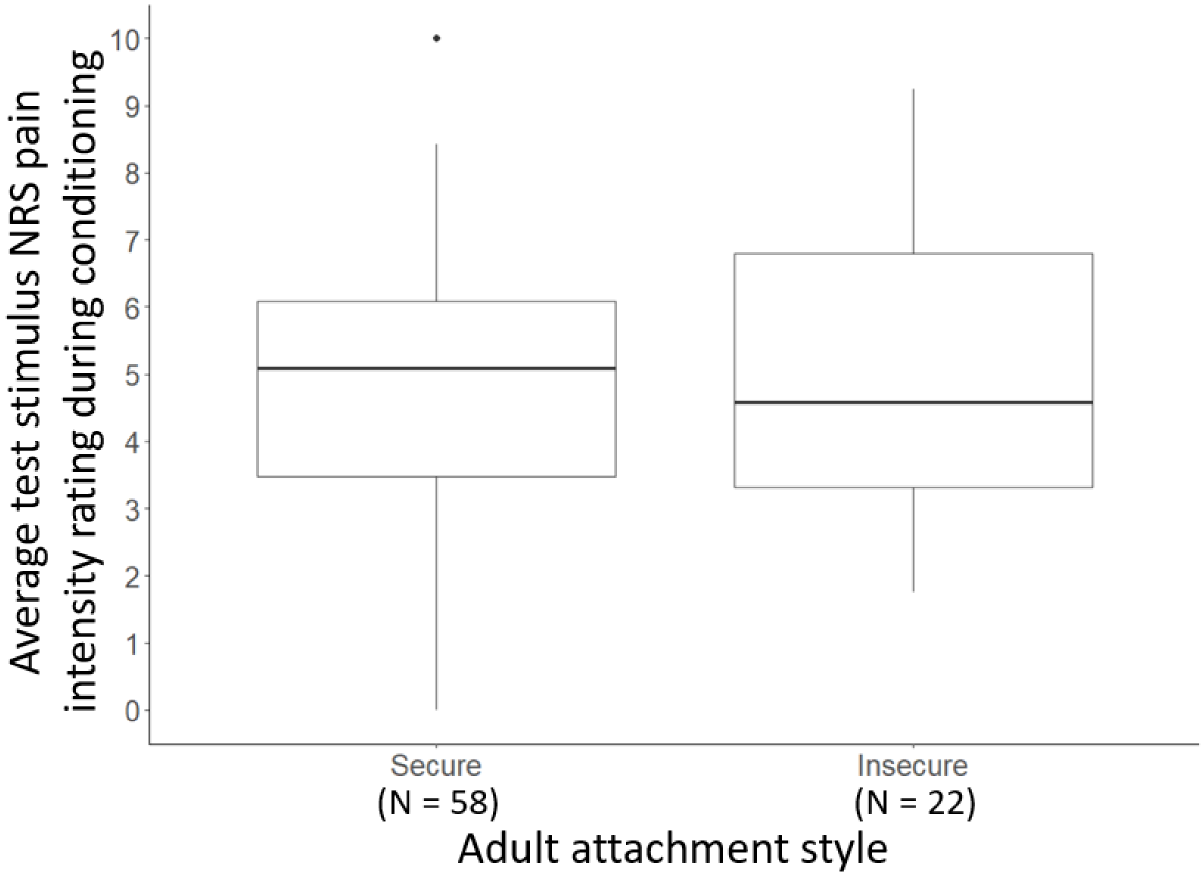

Figure 4.6: The average test stimulus pain intensity rating from the thermode during the conditioning procedure (measured using the Numerical Rating Scale, NRS) for the two overall adult attachment style categories (N=80). *The average test stimulus pain intensity rating during conditioning was calculated by finding the mean for each test stimulus rating during conditioning over the 120 second test stimulus during conditioning phase. The box and whisker plot represents the median and IQR of the average test stimulus pain intensity ratings. The dots in the figure represent outliers in the data.*

To answer the main objective/analysis question, a Welch two-sample t-test model was run to determine the relationship between the two-category adult attachment style and the CPM effect in the 80 (78%) participants who had completed the CPM procedure and therefore had a calculated CPM effect percentage. Out of the 80 participants, eight participants had a CPM facilitatory effect rather than an inhibitory effect, but these individuals were still included in the analysis since the CPM effect variable was analysed as a continuous variable. As such, these 80 participants formed a complete-case model on which I ran my primary CPM analysis. Similarly to the other measures of pain, no association was found between adult attachment style and the CPM effect (t(59) = -0.97, p = 0.338, mean difference [95%CI] = -4.67% [-14.34 – 5.00]) (Figure 4.7).

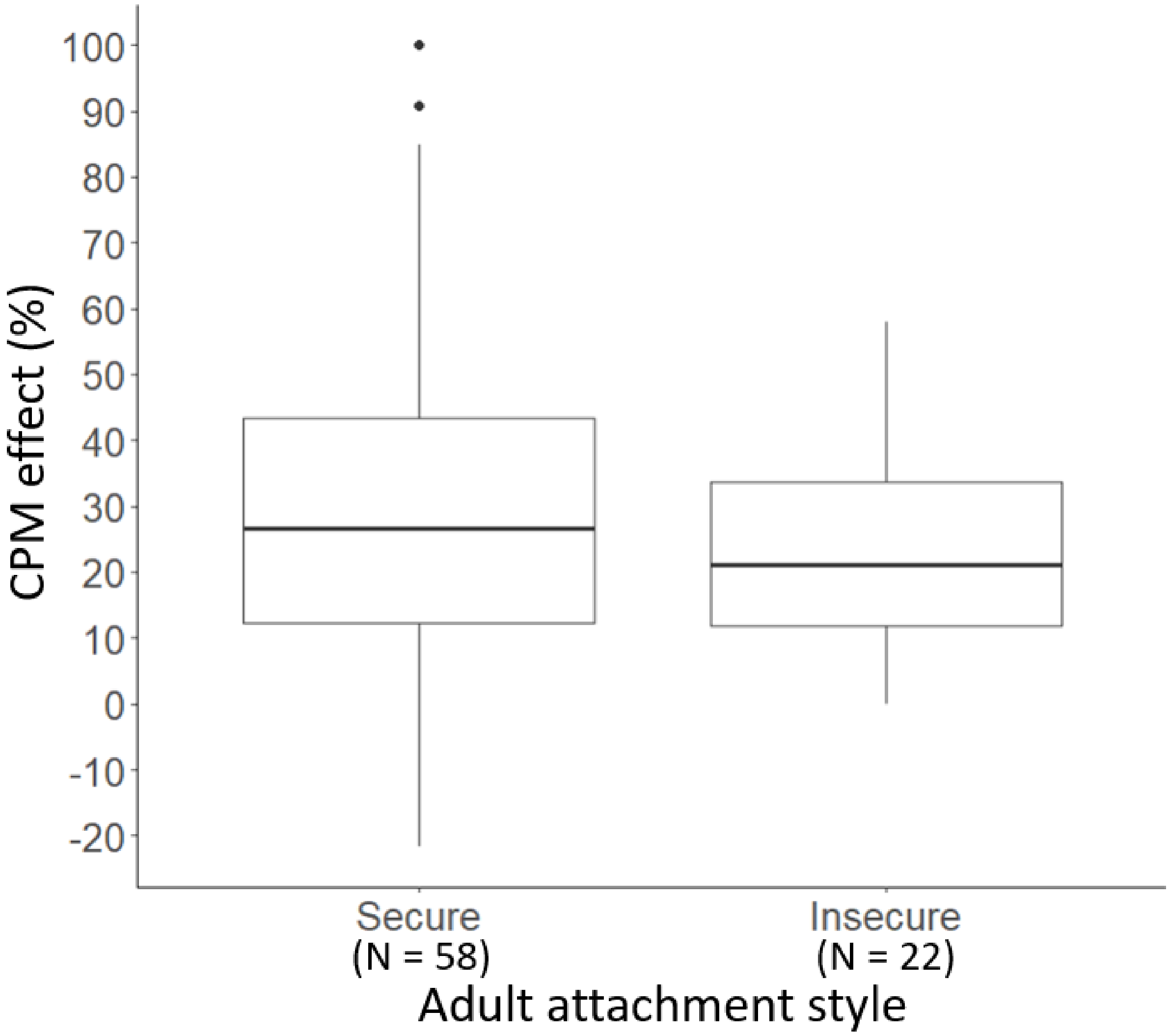

Figure 4.7: The inhibitory effect of the conditioning stimulus for the two overall adult attachment style categories (N = 80). *The CPM effect was calculated by finding the difference between the average test stimulus thermode pain intensity rating and the conditioning stimulus thermode pain intensity rating as a percentage of the average test stimulus thermode pain intensity rating. The negative percentages show pain facilitation in the conditioning stimulus phase, rather than pain inhibition. CPM, conditioned pain modulation. The data in the box and whisper plot represent the median and IQR for CPM effect percentage in the Secure and Insecure participants.*

4.1.2 Exploratory analyses: Are there any associations between adult attachment and the CPM effect when using a multiple imputation model?

Using a complete-case model to assess the relationship between the two broader attachment style categories (Secure vs Insecure) and the CPM effect may reduce precision of estimates and statistical power and may also not be representative of the entire cohort (Mowbray et al., 2022). As such, for a sensitivity analysis a multiple imputation model was used, whereby the missing values of the 23 (22%) participants who did not complete the entire CPM procedure (i.e. did not keep their hand in the conditioning cold water bath stimulus for the full two minutes) were adjusted for in two different ways. For the first imputation method, the last reported thermode pain intensity rating during the conditioning procedure was carried forward for all remaining 10-second unreported intervals. After running a Welch Two-Sample t-test model on all 103 participants, no association between the two-category adult attachment style and CPM effect was found ($t(62) = -1.67$, $p = 0.100$, mean difference [95%CI] = -8.36% [-18.36 – 1.65]). As a second method of imputation, the average test stimulus thermode intensity rating prior to conditioning over the 120 seconds was carried forward to the conditioning phase for the 23 participants who had not completed the CPM procedure. A Welch Two-sample t-test model on these data showed no significant association between the two-category adult attachment styles and the CPM effect ($t(78) = -1.18$, $p = 0.242$, mean difference [95%CI] = -5.15% [-13.85 – 3.54]). These two exploratory analyses forming the multiple imputation model yielded similar results to the complete-case model (both models showed no association between the two-category adult attachment style and the CPM effect), thus increasing my confidence in my results (Mowbray et al., 2022).

4.1.3 Exploratory analysis: Is there an effect of attachment dimensions on threat perception and the CPM effect?

While my aim was to determine the relationship between adult attachment style categories and the CPM effect, as part of my exploratory analyses I looked at the relationship between the adult attachment dimensions (attachment anxiety and avoidance) used in some other papers, and threat perception as well as the CPM effect. The attachment anxiety dimension scores ranged from 1.0 – 5.1 (median [IQR]

= 2.7 [1.8-3.5]) and the attachment avoidance scores ranged from 1.3 – 5.5 (median [IQR] = 3.1 [2.4-3.8]). Threat perception for heat pain was not associated with either adult attachment anxiety (Odds Ratio [95%CI] = 1.05 [0.59 – 1.83], p = 0.872) or attachment avoidance (Odds Ratio [95%CI] = 0.90 [0.45 – 1.66], p = 0.737). Threat perception for the cold pain was also not associated with either adult attachment anxiety (Odds Ratio [95%CI] = 0.72 [0.41 – 1.24], p = 0.237) or attachment avoidance (Odds Ratio [95%CI] = 0.64 [0.34 – 1.15], p = 0.137). Moreover, no significant association was found for either attachment dimension with the CPM effect (Attachment anxiety: Estimate [95% CI] = -3.79 [-8.62 – 1.03], p = 0.122; Attachment avoidance: Estimate [95% CI] = 0.25 [-4.88 – 5.38], p = 0.923).

4.2 Discussion

The main objectives of the experimental part of my research (Part 2) were to determine whether there is a difference between the Secure and Insecure adult attachment style for (1) static measures of thermal pain (pain threshold, tolerance, and single-point intensity), (2) pain intensity over time and cumulative pain load, and (3) CPM effect (a dynamic measure of pain assessing endogenous analgesia and pain inhibitory pathways). My data on 103 individuals in total (73 with Secure attachment and 30 with Insecure attachment) showed (1) no difference in any static measures of pain between the Secure and Insecure attachment styles, (2) no difference in the dynamic measure of pain intensity over time between the Secure and Insecure attachment styles, despite all participants experiencing an increased pain load over time, and (3) no difference in the CPM effect (pain inhibition) between the Secure and Insecure attachment styles – both attachment styles exhibited the CPM effect, showing effective inhibitory pain pathways. Since there were no differences for any of the measures of pain between the Secure and Insecure attachment styles, the Insecure attachment category was not split further into Dismissing, Preoccupied and Fearful styles for the statistical analyses.

My study found no association between adult attachment style and any measures of pain intensity, threshold or tolerance. To my knowledge, there have only been ten other studies that have assessed the relationship between adult attachment and experimental pain perception (Andrews et al., 2011; Hurter et al., 2014; Krahé et al., 2015, 2016; MacDonald, 2008; Meredith et al., 2006a; Mohr et al., 2018; Rowe et al., 2012; Sambo et al., 2010; Wilson and Ruben, 2011). While all of these studies claim some kind of an association between adult attachment and experimental pain, no consistent relationship can be identified. For example, when compared to securely attached individuals most of the studies report a difference in perception of experimental pain in either anxiously- (MacDonald, 2008; Meredith et al., 2006a; Mohr et al., 2018) or avoidantly- (Andrews et al., 2011; Hurter et al., 2014; Krahé et al., 2015) attached (Insecure) individuals with the direction of the difference differing for each protocol. Similarly, a difference in pain perception (either increased or decreased depending on the protocol and outcome measures) in anxiously or avoidantly attached individuals is also reported when compared to the same attachment dimension but in different social contexts (Andrews et al., 2011; Krahé et al., 2015; MacDonald, 2008). Only two studies have found simultaneous associations for both the attachment anxiety and attachment avoidant dimensions with measures of experimental pain (Sambo et al., 2010; Wilson and Ruben, 2011). While the results from these experimental studies are not directly contradictory, the directions of the associations vary depending on the protocol, social context and outcome measures used, resulting in a clear absence of a consistent and predictable relationship between experimental pain and adult attachment style (highlighted also in Table 1.1, Section 1.5.4.1).

The lack of a consistent relationship may be due to several limitations in the study methodologies. Some of studies used the two attachment dimensions instead of the four-category model of attachment to report their results, which neglects cases where both dimensions (belief in self and belief in others) are high (Fearful attachment) or both are low (Secure attachment), introducing a reporting bias (Hurter et al., 2014; Krahé et al., 2015; Sambo et al., 2010). By missing the attachment styles at the two extreme ends, these studies cannot determine a potential additive effect of the attachment dimensions on pain perception, which could particularly impact individuals with a Fearful attachment style. Moreover, the experimental pain models used by the different studies vary, and include: cold pressor tests (response is strongly affected by vascular reactions), thermal pain (the thermode-skin contact can alter the rate of thermal transfer), ischaemic pain (concomitant low-threshold non-nociceptive nerve stimulation, which may inhibit pain mechanisms) and laser-induced radiant heat(high variability in responses) (Reddy et al., 2012). Each of these tests activate different nociceptive fibers and have their own shortcomings (Reddy et al., 2012) and together with my findings that cold pain was viewed as more threatening than the heat pain, the threat level of each experimental pain test may be perceived differently and thus activate the attachment system differently. Many of these studies also created different social contexts by using empathy from a stranger (Sambo et al., 2010) or a romantic partner (Hurter et al., 2014), by having a romantic partner present or absent for the pain procedure (Krahé et al., 2015), by using affective touch (Krahé et al., 2016; Mohr et al., 2018) and by simulating social exclusion (MacDonald, 2008). Each social context could affect the threat appraisal of the experimental pain and could also alter the perceived likelihood of receiving support and eliminating the threat, thus possibly altering the adult attachment system activation. Consequently, while these studies offer intriguing insights into the relationship between adult attachment and experimental pain, the variations in protocols create a challenge in the reconciling the results to establish a definitive link and elucidate underlying physiological mechanisms. The details of these studies and their methodologies are summarised in Table 1.1, Section 1.5.4.1.

Aside from methodological inconsistencies in the kind of pain model and social context used in the attachment and experimental pain studies, there are other caveats, which may further explain the inconsistent results in the literature, as well as the lack of associations between adult attachment style and experimental pain found in my study. I propose two core explanations for my negative results, which I illustrate and summarise in Figure 4.8, and I will expand on throughout my discussion.

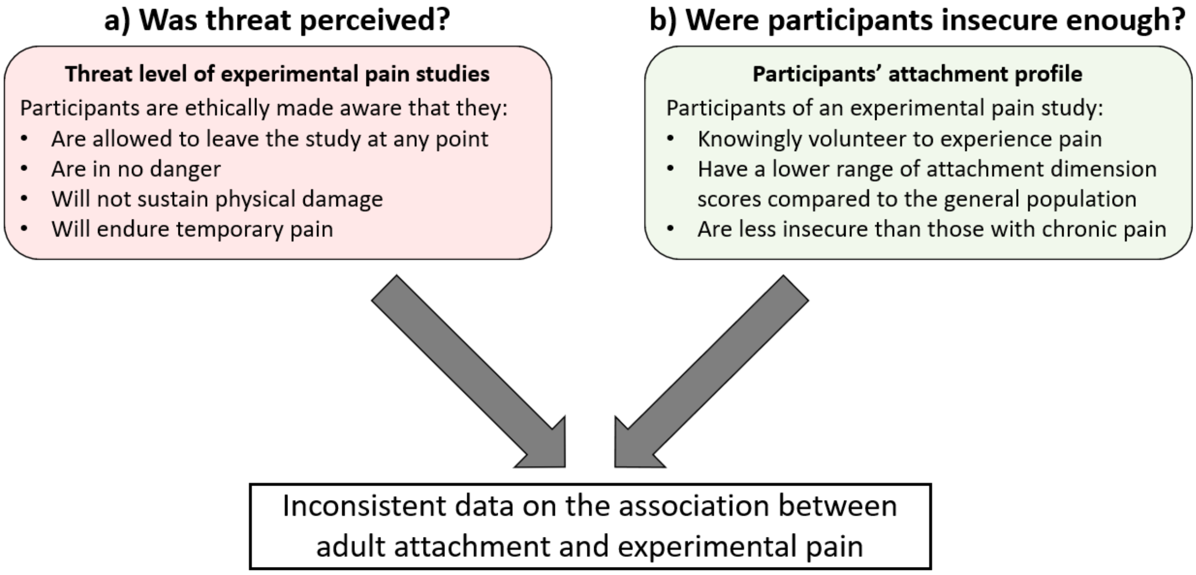

Figure 4.8: A summary of the potential reasons for the negative results in the present experimental pain study. *Reason a) refers to whether participants felt threatened or stressed during the experimental pain procedures (whether the threat comes from the pain, the social environment or the experimenter's manner), because only when threat is perceived is the attachment system activated* (Bowlby, 1969; Mikulincer and Shaver, 2007)*. Reason b) suggests that even if a threat is perceived and the attachment system activates fully, participants in experimental pain studies are not as insecure as those in the general and chronic pain populations* (Mohr et al., 2018)*.*

4.2.1 Was threat perceived?

Perception of a threat is necessary to activate the attachment system and these perceived threats may be social or physical (Bowlby, 1969; Mikulincer and Shaver, 2007). When a threat is perceived, the attachment system first activates on an intrapersonal level, before interpersonal approach or withdrawal behaviours are activated (Mikulincer and Shaver, 2007). The intrapersonal level of attachment activation is when an individual unconsciously appraises the level of the threat based on expectations from previous learned experiences (Bosmans et al., 2020; Mikulincer and Shaver, 2003) and this threat appraisal is affected by flexibility in prefrontal cortex networks (Menon and D'Esposito, 2022). Insecurely attached individuals do not have balance or flexibility between the activation of their left and right prefrontal cortex, reducing the capacity for emotional regulation (Gander and Buchheim, 2015). Individuals with high attachment anxiety display hypervigilance to threat (Ein-Dor, 2014; Mikulincer and Shaver, 2007) due to higher right prefrontal cortex activation, and consequently have a hyperactivation of the attachment system (Rognoni et al., 2008). Individuals with high attachment avoidance display delayed detection of threats

(Ein-Dor, 2014; Mikulincer and Shaver, 2007) due to higher left prefrontal cortex activation, and consequently hypoactivation of the attachment system (Rognoni et al., 2008). Hyperactivation of the attachment system results in the increased presentation of proximity-seeking behaviours while hypoactivation result in the delay of proximity-seeking behaviours (Ein-Dor, 2014; Mikulincer and Shaver, 2007).

From the threat assessment included in the post-experiment questionnaire (Appendix 8), I discovered that less than a quarter of the participants perceived the heat pain as threatening, and just over three quarters of the participants perceived the cold-water stimulus as threatening. These results show that most of the participants only perceived a threat in the final phase of the CPM procedure (that took place in the final 5 minutes of the CPM procedure) rather than during the entire protocol (approximately 40 minutes). In other words, most of the participants only felt threatened in the last 5 minutes of the entire CPM procedure, suggesting a strong likelihood of a delayed activation of the attachment system in my study. Moreover, there was no difference in the threat perception between the Secure and Insecure attachment styles for either stimulus. As such, it is likely that the protocol may not have been threatening enough to consistently activate the attachment system.

Expectation likely played a role in the perception of threat and the subsequent experience of the noxious stimuli (Colloca and Barsky, 2020; Tracey, 2010). All participants were made aware on multiple occasions that neither the heat pain (from the thermode), nor the cold water bath pain would cause any tissue damage, harm or lasting pain. Such disclosures likely reduced the expected threat of the stimuli and likely reduced their expectation of the pain from both stimuli. Indeed, on average, participants reported a lower expected cold pain rating compared to their actual cold pain rating, although no statistical association was found between the expected and actual cold pain rating. A lower perceived threat, be it social or physical, has been found to result in lower expectation of pain and consequent decreased pain intensities, as seen in placebo literature (Colloca and Barsky, 2020; Weimer et al., 2020).

A perceived threat is necessary for the activation of the attachment system, and thus the presentation of attachment behaviours (Bowlby, 1969; Mikulincer and Shaver, 2007), yet of the ten experimental pain studies mentioned above (and summarised in

Table 1.1, Section 1.5.4.1), none specifically performed any objective or subjective measure to confirm increased threat/stress during the pain procedure. Stress responses are one of the ways through which the body responds to a perceived threat (Frisch et al., 2015). As such, stress/threat level may be assessed using physiological measures such as heart rate, salivary cortisol (Kirschbaum et al., 1993), blood pressure (Smeets et al., 2012) or heart rate variability (Kim et al., 2018). One study showed increased heart rate of more than 10 beats per minute during the pain procedure when compared to baseline (Wilson and Ruben, 2011), which is consistent with the literature showing that heart rate increases in experimentally induced stress situations (Hellhammer and Schubert, 2012; Von Dawans et al., 2019; Yao et al., 2016). Another study also measured heart rate but only showed the average heart rate differences (maximum difference of two beats per minute) between different social contexts. They did not provide descriptive statistics for the measured heart rate before and during the pain procedure (Sambo et al., 2010). In this study there was a small increase in heart rate between social contexts (two beats per minute) but, while this change was reported as statistically significant, these increases might not indicate that any of the social contexts were more threatening than the other, since a two-beat per minute heart rate increase does not constitute a stress response (Hellhammer and Schubert, 2012; Von Dawans et al., 2019; Yao et al., 2016). This study by Sambo et al (2010), along with my study, provides some evidence that experimentally induced pain may not be threatening enough for majority of the participants to perceive a threat and consistently activate their attachment system. There are two recent studies, however, investigating how adult attachment moderates the association between experimentally induced secondary hyperalgesia and social support that suggest that the induction of experimentally induced hyperalgesia may induce a stress response (Jaltare et al., 2023, 2024). One study found lower heart rate variability during the induction of secondary hyperalgesia compared to baseline but noted no differences in the heart rate variability between the group that received social support and the group that did not (Jaltare et al., 2023). Similarly, the second study found higher salivary cortisol levels and skin conductance levels when secondary hyperalgesia was induced but there was no difference between the group with support and the group without support (Jaltare et al., 2024). As such, future studies could potentially look at using experimentally induced secondary hyperalgesia protocols when investigating associations between adult attachment and measures of pain, since they may be more threatening and thus likely to activate the adult attachment system.

In patients with chronic pain, the threat of pain persists and often is difficult to resolve (Aldrich et al., 2000; Elman and Borsook, 2018; Timmers et al., 2019). Chronic pain likely activates the attachment system in a way that may not be reproduceable in the experimental pain setting. Chronic pain is often also intertwined with complex psychosocial factors, including depression, anxiety, pain catastrophising, stress, social expectations, self-efficacy, cognitive beliefs and learned fears (Cohen et al., 2021; Edwards et al., 2016). As such, even if experimental pain protocols are threatening enough to activate the attachment system, they may not be able to fully recreate the experience of chronic pain due to the psychosocial complexities accompanying chronic pain. Still, threat can be induced and measured in an experimental context by using approved stress test protocols (such as the Trier Social Stress Test (Frisch et al., 2015; Kirschbaum et al., 1993) and the Maastricht Acute Stress Test (Smeets et al., 2012)) that have been developed to consistently simulate a stress response. The induction of stress from any type of stress test can, and should be, confirmed by measuring objective physiological variables such as heart rate (Kirschbaum et al., 1993; Yao et al., 2016), heart rate variability (Kim et al., 2018), blood pressure (Smeets et al., 2012) or salivary cortisol (Kirschbaum et al., 1993; Smeets et al., 2012) before, during and after the stress test.

Aside from the two studies on the moderating effect of adult attachment on the association between experimentally induced secondary hyperalgesia and social support (Jaltare et al., 2023, 2024), no studies investigating the association between adult attachment and experimental pain measures explicitly assess stress/threat when pain is experimentally induced. There are, however, studies assessing the relationship between experimentally induced stress and adult attachment. These studies report that physiological arousal (measured using heart rate, heart rate variability and/or electrodermal activity) is increased in response to stress for insecurely compared to securely attached individuals (Bryant and Hutanamon, 2018; Gander et al., 2022; Roisman, 2007). However, there are some caveats in these studies that need to be acknowledged: 1) these studies do not use any official stress test protocol (Bryant and Hutanamon, 2018; Gander et al., 2022; Roisman, 2007) and 2) only one study confirmed an overall stress response by looking at the difference between the physiological measures at baseline and during the stress responses, before accounting for attachment, social context or condition (Gander et al., 2022). As such, there is evidence that stress responses differ depending on adult attachment style, although no studies, to my knowledge, have determined a stress/treat threshold necessary for attachment system activation. Possibly, future studies could explore whether the use ofobjective measures of stress can be used to determine whether a threat “threshold” exists for the consistent activation of the attachment system throughout experimental procedures and whether these potential “thresholds” differ between attachment styles. Without first ensuring that the attachment system is activated, the results from experimental pain are difficult to interpret clearly and cannot be generalised to the broader and clinical populations, where pain is not predictable and does not occur in a controlled environment.

Moreover, if threat is perceived and the attachment system is activated on an intrapersonal level, the presentation of the types of interpersonal behaviours would depend not only on the attachment styles but also likely the social context in which the pain is experienced (Mikulincer and Shaver, 2007). If there is a chance of receiving support (i.e. there is a person or people present and they appear willing to offer support) then proximity-seeking behaviours are likely for individuals with high attachment anxiety but unlikely for individuals with high attachment avoidance (Mikulincer and Shaver, 2007). Conversely, when nobody is present or it seems unlikely that they will offer support, there may be a decrease in proximity-seeking behaviours for individuals with high attachment anxiety (due to fear of rejection) but individuals with high attachment avoidance will likely be less affected since they rely more on autonomy than external support (Mikulincer and Shaver, 2007). As such, even if threat is detected, the social context is which the threat occurs may alter the presentation of attachment behaviours.

4.2.2 Was the participants’ attachment insecurity high enough?

The median attachment anxiety and attachment avoidant scores from the attachment dimensions of the participants in the experimental study (Section 4.1.3) were higher than the corresponding medians from the pain-free female participants from the survey

(Section 3.1.2). Despite the higher medians for attachment anxiety and avoidance in the experimental cohort, none of the participants had a maximum score (a score of 7) for either attachment anxiety or attachment avoidance. Whereas participants from the equivalent group in the survey (female, pain-free, covering all attachment styles) had maximum attachment anxiety scores (a score of 7) and just below maximum (a score of 6.1) attachment avoidance scores. The comparison of the range of attachment dimension scores from my experimental compared to survey study are summarised in Figure 4.9B, including a comparison to the range of dimension scores seen in the pain-free female participants who initially volunteered to participate in the experimental study. Other studies have also found that the mean scores for attachment anxiety and attachment avoidance were lower in their experimental pain cohort when compared to the general population (Krahé et al., 2015; Mohr et al., 2018). These results demonstrate a possible sample bias, and interestingly may provide important evidence that individuals who are likely to volunteer for and, especially, participate in, experimental pain studies have lower levels of attachment anxiety and avoidance when compared to the general population. Accordingly, even if the experimental pain protocols are threatening enough to activate the attachment system (by using a stress test to increase the likelihood of activating the attachment system), the participants in the experimental pain studies may not have the full range of attachment dimension scores. Without the full variability in the dimension scores, the experimental pain participants may not be "insecure enough" to see a difference in the response to the painful stimuli even if their attachment system is activated, making it difficult to evaluate true associations between attachment and experimental pain.

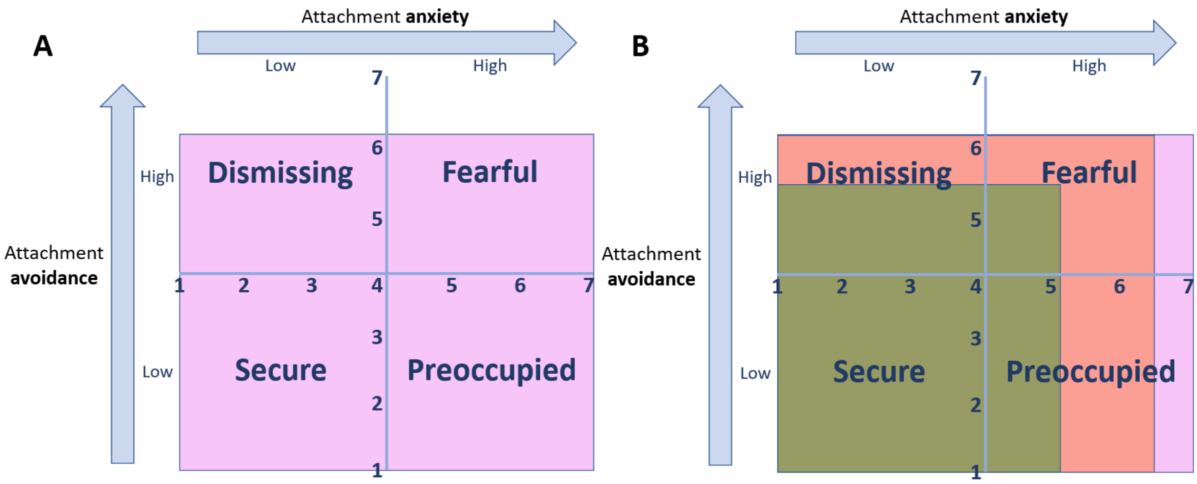

Figure 4.9: A comparison in the attachment dimensions scores for the pain-free female population in the survey, the pain-free females who volunteered to participate in the experimental pain study and the pain-free females that made up the final experimental pain cohort. *Panel A shows the standard attachment dimension scores (both attachment anxiety and avoidance range from 1 – 7) and attachment style quadrants. The dimension scores are offset slightly to the left of the y-axis and to the bottom of the x-axis to visually show that a score equal to four would be classified as Secure on both dimension scales* (Fraley et al., 2011)*. Panel A also shows a visual representation (pink square) of the distribution of attachment dimensions scores (anxiety: 7, avoidance: 6.1) for the pain-free female portion of the survey study. Panel B has the same components of panel A but overlaid with the range of dimension scores for the pain-free females from the survey who volunteered to participate in the experimental study (orange square) and my pain-free female experimental study participants (green) – i.e. those who volunteered and followed through with participation. The cohorts differ between those who volunteered and those who participated because not all individuals who volunteered followed through with participation. The maximum attachment anxiety score for the pain-free female survey population was 7 (the maximum possible score for either attachment dimension), with the maximum attachment anxiety score for the volunteers was 6.5, while the maximum attachment anxiety score for the experimental participants was only 5.1. The pain-free females in the survey and in those who volunteered to participate in the experimental study had a maximum attachment avoidance score of 6.1, while the attachment avoidance score for the pain-free female participants was even lover at 5.5.*

Lastly, the majority of other experimental pain and attachment studies, do not report the descriptive statistics of the attachment dimension scores, or only report attachment in the four attachment styles, making it difficult to determine the relative security/insecurity of the participants in each of the ten studies previously discussed. It may benefit future studies to report and analyse their data in both the attachment dimensions and in the adult attachment style categories to ensure that a quantitative measure of the extent of attachment insecurity in included (Fraley et al., 2015).

4.2.3 Limitations, strengths and future directions

Some limitations and strengths of my experimental study should be acknowledged. To account for the effects of social context on the perception of pain (Krahé et al., 2013; Piedimonte et al., 2021; Stanke and Ivanec, 2010), my study was designed to have all experimental procedures performed in a small air temperature-controlled room that was isolated from other people. Unfortunately, due to laboratory renovations, for approximately the second quarter of my participants, the location of the procedure needed to change to a larger laboratory that was not completely isolated from other people, such that the social context was not uniform for all participants. Moreover, the cohort for the experimental part of the study consisted predominantly of undergraduate university students, mostly from the Faculty of Health Sciences, who were thus familiar with the health science campus and the building where the experiment took place. This poses two factors to consider: 1) the sample was fairly homogenous and not representative of the general population, and 2) the familiar environment, may have further reduced the overall threat-value of the experiment. Future studies could consider using a more diverse sample for their cohorts by advertising through social media platforms and minimizing the number of participants familiar with the department, building and laboratory used. The cold pain stimulus may have acted as a distraction, reducing the reported thermode test stimulus intensity during the conditioning procedure, however a previous study (that used contact heat as the test stimulus and cold water as the conditioning stimulus) showed an additive effect of distraction and CPM (Moont et al., 2010). This study suggested separate physiological mechanisms underlying distraction and CPM, making my CPM effect results unlikely to be due to distraction. Furthermore, the CPM procedure, while reliable (Kennedy et al., 2016), does give rise to inter-individual variability in the CPM response profiles (Ramaswamy and Wodehouse, 2021). Participants were also not screened with an initial CPM procedure to determine which participants would likely display an inhibitory pain effect of the conditioning cold pain stimulus on the test stimulus pain intensity during conditioning. However, only eight participants of 80 did not have the CPM inhibitory effect, and the CPM effect variable was analysed as a continuous variable, which should have maintained the integrity of the results. Still, the CPM procedure provides a reliable way of measuring endogenous analgesia in an experimental setting (Kennedy et al., 2016; Ramaswamy and Wodehouse, 2021). I also followed a previously tested protocol that used a cold water bath as the conditioning stimulus (Lie et al., 2017), which is the most commonly used conditioning stimulus in CPM procedures (Kennedy et al., 2016). The protocol that I followed also used contact heat as a test stimulus, which has been reported to be the second most used test stimulus, after pressure pain threshold, in CPM procedures (Kennedy et al., 2016). Individualised heat temperatures used as the test stimulus have shown fair to excellent reliability (Kennedy et al., 2016), which is why I chose contact heat as the test stimulus.

To remain blinded to the attachment style of the participants, no attachment styles were scored or classified prior to the experimental procedure. As a result, I remained unbiased, which is a study strength, but at the same time I could not ensure that each attachment style was adequately represented, or that the participants spanned the full range of the attachment anxiety and attachment avoidant dimensions (from lowest to highest dimension scores). In the end, of the 103 participants, 73 were Secure while only 30 were Insecure (Dismissing: 14, Preoccupied: 6, Fearful: 10). Although my study is the largest experimental study on attachment and experimental pain that I know of, the group sizes may still be too small to detect any differences given the number of subjective factors that can influence pain perception. Moreover, participant recruitment may introduce an innate bias with mostly securely attached individuals participating. To possibly increase the representation of Insecure attachment styles in experimental pain studies, future studies could look at using two investigators: one to invite participants and score the attachment questionnaire prior to participation, and another to run the experimental procedure whilst remaining blinded to the attachment style of the participant.

I used one of the various available standardised protocols to assess CPM, in which tonic heat pain was used as the test stimulus (experienced from a thermode positioned on the right distal volar aspect of the forearm) and cold pain was used as a conditioning stimulus (experienced in the left hand that was submerged in a cold water bath) (Lie et al., 2017). Although this CPM protocol was effective in inducing endogenous analgesia in the participants overall, (as shown by the decreased conditioning stimulus compared to the test stimulus pain intensity rating), it is possible that different test and conditioning stimuli may have produced different results (i.e. the magnitude of the CPM effect as a measure of pain inhibition) (Ramaswamy and Wodehouse, 2021). Indeed, a study using three different conditioning stimuli (ischaemic pain and cold pain using a cold water bath and heat pain using a thermode) found that the CPM effect size was significantly different for each stimulus (Aparecida Da Silva et al., 2018). A pressure pain test stimulus and a cold pressor pain conditioning stimulus is reported to yield the largest CPM effect (Ramaswamy and Wodehouse, 2021), which might therefore more easily detect any differences between groups. For the CPM procedure, however, there is currently no standard protocol established for assessing the CPM effect (as a measure of pain inhibition), with multiple different CPM procedures (using difference test and conditioning stimuli) being used (Aparecida Da Silva et al., 2018; Ramaswamy and Wodehouse, 2021). Due to the lack of uniform methodology in attachment and experimental pain research, including inconsistent pain modalities and varied social contexts, a future direction for the field could be to conduct a systematic analysis of the reliability and limitations of the data yielded by each CPM procedure as well as the pragmatic feasibility of each procedure, concluding with a suggestion for the best CPM procedure to adopt in future studies.

Given the reported effect of experimenter manner on pain perception, where the experimenter’s increased confidence and professionalism has been found to result in decreased reported pain intensity (Daniali and Flaten, 2019), I used a standardised script (Appendix 4) in an attempt to maintain a neutral/professional manner for all participants. While 20 of the 103 participants perceived my manner as “friendly”, the majority of the participants did perceive my manner as the desired neutral/professional. For the reasons discussed above, my protocol may not have been threatening enough to activate the adult attachment system. It may, therefore, be beneficial for future studies looking at the association between adult attachment and experimental pain to also ensure that their protocols are threatening/stressful enough to activate the attachment systems. Perhaps the first step that could be taken by future studies would be to determine if there can be a measure for the threshold of perceived threat necessary to activate the attachment system. If such a threshold exists, it would have many implications for attachment research in the context of pain as it would allow researchers to better study and understand the different levels of activation, as well as ensure that the attachment system is consistently activated in an experimental pain procedure. Moreover, it would aid in developing experimental pain procedures that are threatening enough to activate the attachment system whilst ensuring that participants are not exposed to unethical physical or psychological risks. Additionally, future studies could investigate other potential mechanisms underlying the possible increased risk for the development of chronic pain; One possible mechanism worth exploring could be pain catastrophising. Certainly, for meaningful interpretation and understanding of the relationship between attachment and experimental pain, future studies require standardised methodology of the modality and social context used in experimental procedures.

Despite the limitations, there are some noteworthy strengths of my study that should be acknowledged. To my knowledge, I had the largest experimental pain cohort in the context of experimental pain and adult attachment (103 participants compared to 39-95 participants in the other ten studies (Andrews et al., 2011; Hurter et al., 2014; Krahé et al., 2015, 2016; MacDonald, 2008; Meredith et al., 2006a; Mohr et al., 2018; Rowe et al., 2012; Sambo et al., 2010; Wilson and Ruben, 2011)) as well as in the context of CPM (other CPM study cohorts range from 20 – 72 participants (Bjørkedal and Flaten, 2012; Harrison et al., 2022; Ibancos-Losada et al., 2020; Lewis et al., 2012; Lie et al., 2017; Nir et al., 2012, 2011)). Moreover, I was the first to experimentally assess the mechanisms of different pain experiences for different attachment styles through a model of endogenous analgesia. Previous studies looking at the association between pain and adult attachment did not look at possible mechanisms of pain, but rather examined static measure of pain including pain threshold, tolerance and single-point intensity (Andrews et al., 2011; Hurter et al., 2014; Krahé et al., 2015, 2016; MacDonald, 2008; Meredith et al., 2006a; Mohr et al., 2018; Rowe et al., 2012; Sambo et al., 2010; Wilson and Ruben, 2011). Investigating possible mechanisms behind pain may be valuable in explaining the associations between adult attachment and chronic pain, and better understanding the complex, personal experience of chronic pain.

4.2.4 Conclusion

My experiment investigated the relationship between adult attachment styles and experimental pain perception, using both static and dynamic measures of pain and endogenous analgesia. This is the largest experimental pain cohort investigating adult attachment and the CPM model, as an assessment of endogenous analgesia. My findings showed no significant difference between Secure and Insecure attachment styles across these various measures of pain and pain inhibition. Other experimental pain and attachment studies have displayed a lack of a consistent relationship, potentially stemming from methodological discrepancies like varying pain induction methods, differential use of attachment categorisations, and divergent social contexts. My data support those of others (Bedwell et al., 2022) and imply that experimental pain procedures may not consistently evoke perceived threats in the context of the attachment system, thereby inconsistently activating the attachment system. Indeed, my data indicate that most participants only perceived threats during the last 5 minutes of the protocol. Furthermore, lack of variability in attachment dimension scores may bias results towards null findings, potentially failing to capture the true relationship between attachment and pain perception, should it exist. For future research, it is imperative to address these methodological inconsistencies and potential biases. Incorporating objective stress measures to ensure the consistent activation of the attachment system, and aiming for a representative range of attachment styles is crucial. In conclusion, my study provides valuable insight into the constraints of current experimental pain and attachment studies and offers a nuanced perspective into the intricate relationship between adult attachment and experimental pain perception.

CHAPTER 5

CONCLUSION

5.1 Summary of the literature in the field of pain, threat and adult attachment

This study came about following an interest in the effect that past experiences and subsequent expectations can have on the perception of pain to better understand the factors that increase an individual's risk for developing chronic pain. Chronic pain is a complex experience that is entirely subjective and personal (Raja et al., 2020). Coupled with its complexity, the global burden of chronic pain is substantial, with chronic pain prevalence in developed countries ranging from 11% - 43% (Cohen et al., 2021) and chronic pain prevalence in developing countries ranging from 13% - 51% (Sá et al., 2019). A recent nationally representative sample of South Africans found that the prevalence of chronic pain in South Africa was 18%, with an increased chronic pain prevalence of 20% in women (Kamerman et al., 2020). Coupled with the high prevalence of chronic pain (27%) found in my first study, these studies underscore the significance of the global and local burden of chronic pain and emphasise the need to better understand the possible risks leading to the development of chronic pain.

The importance of threat, both physical and social, and its significant impact on pain perception has been highlighted as a key theme throughout my thesis. Early interactions with primary caregivers shape individuals' responses to threat and lay the groundwork for adult attachment styles, which subsequently govern behavioural responses to these perceived threats, including pain (Mikulincer and Shaver, 2007). Moreover, expectations that are created by past experiences and learnt responses have been found to influence the perception of threat and subsequently pain (Colloca and Barsky, 2020; Petrini and Arendt-Nielsen, 2020).

Importantly, the significance of the social aspect of pain has been emphasised in a recent review, calling for a reappraisal of the biopsychosocial model (Nicholas, 2022) to what has been called a "sociopsychobiological model" (Mardian et al., 2020) (Figure 5.1). This new perspective underlines that pain is not just a personal physical experience with psychological contributions and consequences but is deeply embedded in social contexts. It necessitates a shift from the traditional biopsychosocial model, suggesting a reorientation where social aspects form the foundation of pain (Nicholas, 2022). This approach aligns with my studies' emphasis on adult attachment styles, which are inherently shaped by past interpersonal interactions (Bowlby, 1969; Mikulincer and Shaver, 2007).

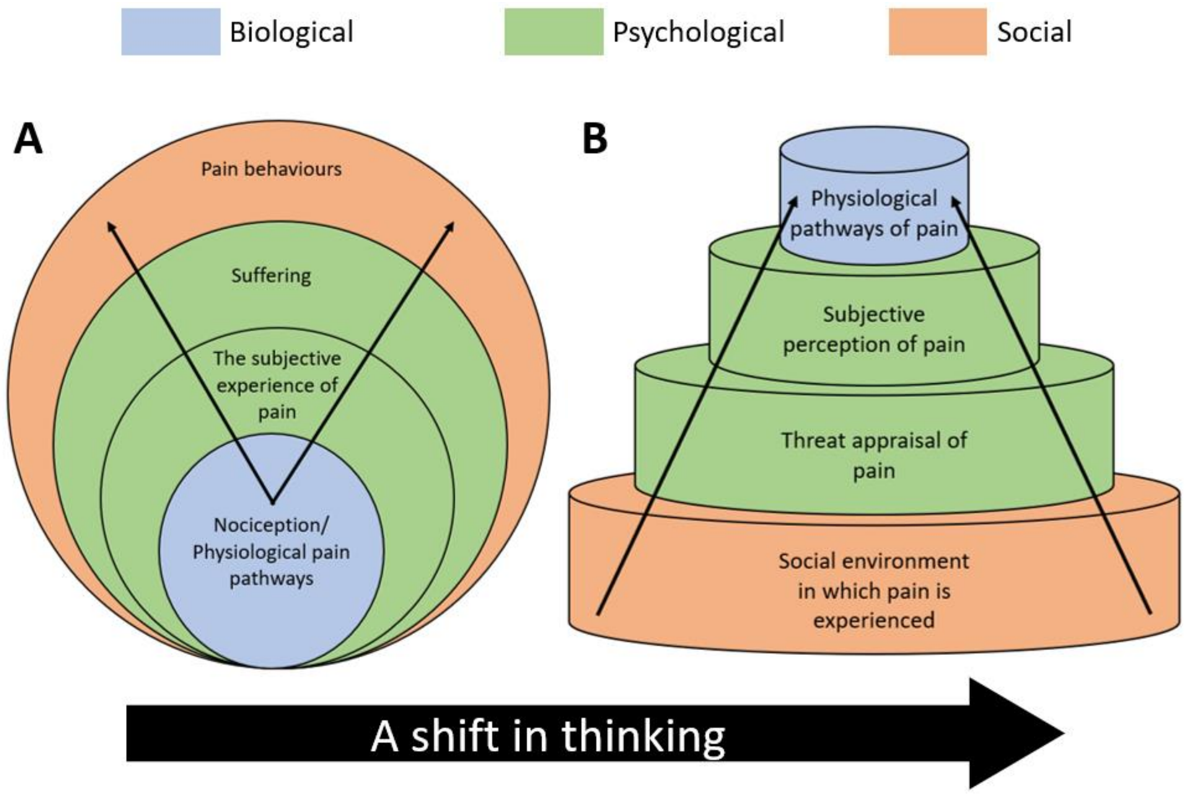

Figure 5.1: A shift in thinking away from a biopsychosocial model towards a sociopsychobiological model of pain. *Diagram A shows the biopsychosocial model of pain* (Loeser, 1982)*. In diagram A, the physiological pathways of pain are seen as the core component of pain. Diagram B depicts my representation of the sociopsychobiological mode argued by Nicholas in 2022. In diagram B, the social environment in which pain is experienced is the foundation of pain. The sociopsychobiological model emphasises the importance of considering the substantial impact that the social context has on pain* (Carr and Bradshaw, 2014; Mardian et al., 2020; Nicholas, 2022)*.*

5.2 Summary of my findings

My research investigated the relationship between adult attachment style and chronic pain prevalence and between adult attachment style and perception of experimental pain and endogenous analgesia in a South African population. Both studies provide insightful findings into the complex relationship between adult attachment styles and pain, both chronic and experimentally induced; a largely unexplored field. The first study, involving a nationwide online survey in 2371 participants, revealed a significant association between Insecure attachment styles and the prevalence of chronic pain. In this young (median age 23 years; IQR 20-28), predominantly female (74%) cohort, those with Insecure attachment styles had a higher chronic pain prevalence when compared to securely attached individuals; with the Fearful adult attachment style remarkably having more than double the chronic pain prevalence when compared to Secure attachment. In line with other studies (Andersen, 2012; Davies et al., 2009; Kowal et al., 2015; Meredith et al., 2007), the burden of pain, measured in terms of pain intensity, interference, and number of pain sites, was not directly associated with adult attachment styles. Instead, and importantly, my data show that the relationship between attachment and chronic pain burden is mediated by pain catastrophising, suggesting a psychological component in the relationship between attachment style and chronic pain and emphasising the role of threat perception in the progression of chronic pain. This is the first report showing this mediating effect of pain catastrophising, and my data support and highlight the impact of psychosocial factors, such as attachment styles shaped by early life experiences, on the physical experience of pain in adulthood.

Data from my second study, involving the experimental assessment of pain and endogenous analgesia, presents a somewhat different picture. I found no significant association between Secure and Insecure adult attachment styles and various measures of pain intensity, threshold, tolerance or endogenous analgesia (measured by looking at the CPM effect). This lack of association between adult attachment and the CPM effect persisted even after accounting for missing values through a multiple imputations model. The results from the second study may serve to highlight the difference in chronic vs experimental pain, and also that experimental pain procedures might not consistently activate the attachment system, which requires the perception of threat. Although others have reported an association between adult attachment and experimental pain (Andrews et al., 2011; Hurter et al., 2014; Krahé et al., 2015, 2016; MacDonald, 2008; Meredith et al., 2006a; Mohr et al., 2018; Rowe et al., 2012; Sambo et al., 2010; Wilson and Ruben, 2011), no consistent direction of effect or association can be identified, possibly due to methodological differences and the high possibility that the experimental procedures and social contexts differ vastly from study to study and may not be threatening enough to activate the attachment system.

Figure 5.2 summarises potential issues with current experimental pain and attachment studies, suggesting that it would be beneficial for future studies to establish an association between adult attachment and experimental pain in a neutral social context first, before investigating how the social context can influence this relationship. However, there are challenges that need to be overcome to answer the research question in Step 1 of Figure 5.2. These challenges include ensuring that the experimental pain protocol is threatening enough (either physically or socially) to increase the likelihood of a uniform adult attachment system activation and taking steps to possibly increase the range of adult attachment dimensions represented in the experimental cohort to decrease the bias of the sample. Until these challenges have been overcome and the research question in Step 1 can be answered, CPM should not be ruled out as a possible mechanism for the increased chronic pain prevalence in individuals with an Insecure, compared to a Secure, adult attachment. That being said, with the relationship between adult attachment style and chronic pain burden being mediated by pain catastrophising in my first study, it follows that a possible mechanism behind the increased chronic pain prevalence in insecure attachments may be cognitive in nature, which could provide a worthwhile avenue for further research.

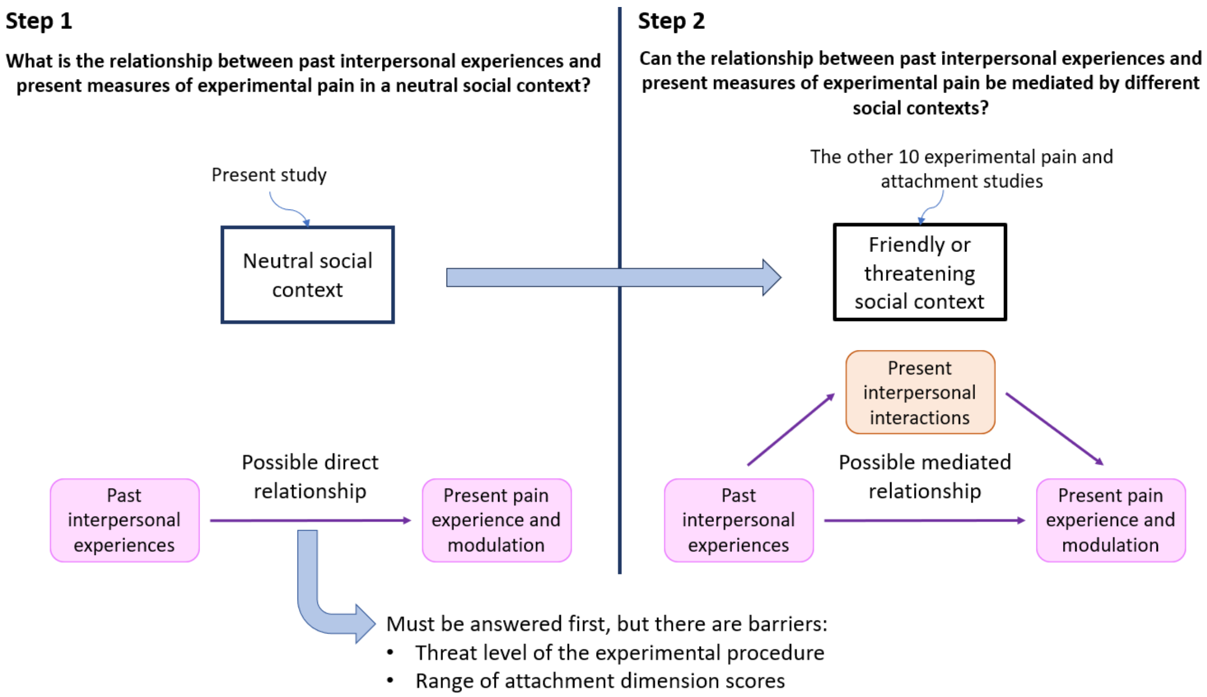

Figure 5.2: A diagram showing two different research questions and processes in the exploration of the effect of attachment style on pain. *The ten other studies looking at the association between adult attachment and experimental pain, were investigating a mediated relationship through present interpersonal interactions* (Andrews et al., 2011; Hurter et al., 2014; Krahé et al., 2015, 2016; MacDonald, 2008; Mohr et al., 2018; Rowe et al., 2012; Sambo et al., 2010; Wilson and Ruben, 2011)*, or did not specifically control the social context either way, or ensure that the social context was kept constant/controlled* (Meredith et al., 2006a). *I suggest, however, that the primary research question in Step 1 needs to be answered first, before a mediated relationship can be studied. Step 1 summarises the direct association between past interpersonal interactions (which are measured through adult attachment styles) and the present experience of experimental pain. My study was investigating this direct relationship. The limitations that need to be overcome to determine the relationship in Step 1, however, include ensuring that the experimental procedure is threatening enough to activate the attachment system and that the participants cover the full range of attachment dimension scores.*

Both the survey (Part 1) and experimental procedure (Part 2) had noteworthy study strengths and limitations (detailed in Sections 3.2.1 and 4.2.3) that may help to inform future research in the field of adult attachment and pain (further discussed in the next section). First, both studies had large cohorts when compared to other similar experimental and chronic pain studies looking at adult attachment. In Part 1 of my thesis, I was also the first to assess the relationship between chronic pain prevalence and adult attachment, whereas previous studies have looked at the prevalence of each adult attachment style in individuals who already have chronic pain (Davies et al., 2009). Although I did find an association between adult attachment style and chronic pain prevalence, no causal relationships can be inferred due to the cross-sectional nature of the study, and future studies may benefit from looking at the association between adult attachment style and chronic pain incidence. In the second experimental study, I was the first to assess the mechanisms of different pain experience for different attachment styles through a model of endogenous analgesia. Despite my negative data with regards to a relationship between experimental pain perception and attachment style, and pain inhibition and attachment style, I still believe that an understanding of the association between adult attachment styles and pathways of endogenous analgesia may provide some insight into one of the possible mechanisms that may contribute to vulnerability of developing chronic pain in insecurely attached individuals; as supported by my results that Insecure adult attachment styles are associated with increased chronic pain prevalence, and that the relationship between Insecure adult attachment styles and an increased burden of chronic pain is mediated by pain catastrophising.

5.3 Possible implications and future research

Though I recognise the limitations in attachment research, including my own study's, I believe that attachment styles offer a measure of an individual's underlying beliefs/expectations around safety or danger in perceived socially (or non-socially) threatening situations, and may therefore also offer a measure of predicted directed behaviours during such threatening situations. Future studies could look at the incidence of chronic pain for different adult attachment styles within a population to determine if individuals with insecure attachment styles are at greater risk of developing chronic pain compared to individuals with Secure attachment, as my prevalence data suggest. Moreover, future studies could investigate the effect of increasing chronic pain burden on attachment styles over time and *vice versa* to shed more light on the possible direction of association. For experimental studies moving forward, more standardised approaches with respect to experimental pain protocol and social context are needed to determine if consistent associations between adult attachment style and experimental pain exist. While my study does not exclude CPM as a possible mechanism for the increased chronic pain prevalence in insecurely attached individuals, and further studies are needed to confirm the association or lack thereof, future studies should also explore other potential mechanisms for this association. One promising avenue to explore could be pain catastrophising since it mediated the association between adult attachment style and chronic pain burden. Could addressing pain catastrophising cognitions through cognitive restructuring strategies and physical exercise (Petrini and Arendt-Nielsen, 2020) alter the perception of experimental and chronic pain, particularly in individuals with an insecure attachment style? Additionally, experimental pain studies could explore behaviours that are common between those expressed in experimental and chronic pain and those expressed following the activation of the attachment system as another way of establishing a link connecting these two factors, possibly further emphasising the importance of considering adult attachment in pain research.

More experimental research is also needed in different populations, including people with less education and lower socioeconomic statuses. Insecure adult attachment styles are associated with lower socioeconomic status (Sakman et al., 2022), so a sample obtained from a population with low socioeconomic status may include a higher proportion of individuals with insecure attachment. As such, these samples may include participants with enough attachment insecurity to see possible differences in pain reporting and modulation between securely and insecurely attached individuals. Whilst a higher proportion of insecure attachment and potentially higher pain prevalence may have a benefit in answering the research question, it would also mean the impact of the research could be greater if more people were affected by pain. What role could pain catastrophising have on pain in a sample with lower levels of education and socioeconomic status? Could adult attachment style have a greater effect on the prevalence of chronic pain in a sample with richer social interactions? In the following paragraphs, I look at the broader picture and discuss the implications and future of attachment and pain research more generally as a way of providing an overall view of my study in the context of the greater literature.

The psychological vulnerability of insecurely, compared to securely, attached individuals with chronic pain is highlighted through the mediating effect of pain catastrophising in the relationship between adult attachment style and the burden of chronic pain. My finding adds to previously published data that showed that individuals with an Insecure adult attachment have poorer psychological outcomes, including decreased self-efficacy and increased depression, anxiety and pain catastrophising, following pain management strategies compared to those with a Secure attachment style (Andersen, 2012; Ciechanowski et al., 2003; Kowal et al., 2015; Meredith et al., 2007). The mediating effect of pain catastrophising also emphasises the roles that threat perception and attention to the threat of pain play on the progression of chronic pain. From a social aspect, the engagement with pain management programmes and support seeking behaviours has been found to differ depending on one's belief in self vs belief in others (Belot et al., 2021; Kowal et al., 2015; Nasika et al., 2023). Individuals with a low belief in others may show hesitancy when seeking treatment for their pain due to their lack of trust in the healthcare practitioners, while individuals with a low belief in self may engage in treatment initially but do not always follow through (Belot et al., 2021; Brenk-Franz et al., 2015; Mikail et al., 1994). As such, the importance of understanding the psychosocial aspect of the relationship between adult attachment and chronic pain is evident. The biological/physiological aspect to the pain perception for the different attachment styles is also important and still should be investigated further. Despite my negative data, the functioning of pain inhibitory pathways may be different for different adult attachment styles. The increased prevalence of chronic pain in individuals with an Insecure, compared to a Secure, adult attachment style, highlights the possibility that attachment insecurity may be one of the possible risk factors for developing chronic pain, and the importance of understanding possible mechanisms, such as differences in endogenous analgesia, for this vulnerability becomes apparent.

With the advent of social media, adult interpersonal interactions have transformed, warranting investigation into how modern social/interpersonal dynamics influence attachment formation and change over time, as well as the consequent pain experiences. This exploration could reveal whether increased online interactions enhance attachment security or if the decline in face-to-face interactions adversely affects it. Understanding these psychosocial facets is crucial as pain is intrinsically a personal experience (Raja et al., 2020), and individual responses to experimental pain (Meredith, 2013), chronic pain (Davies et al., 2009; Meredith et al., 2008) or pain management programmes (Andersen, 2012; Kowal et al., 2015) might be better comprehended through the lens of adult attachment styles.

My research presents insights into the complex interplay between adult attachment styles and pain in a South African cohort. The first study, which unveils a significant association between Insecure attachment styles and higher chronic pain prevalence, further identifies the mediating role of pain catastrophising in the association of Insecure adult attachment styles with the higher burden of chronic pain. These findings indirectly highlight the influence of early life experiences and psychosocial factors on adult pain perception. In contrast, the second study reveals no association between attachment styles and experimental pain measures. This discrepancy underscores the difference between chronic pain and experimental pain and the need for more standardised methodologies in experimental pain and attachment research. Overall, my project has spotlighted attachment insecurity as a potential risk factor in the development of chronic pain. My research underlines the importance of considering social contexts and interpersonal interactions in understanding these complex pain experiences, especially in the contemporary era of evolving social media dynamics. Moreover, the mediating effect of pain catastrophising in the relationship between adult attachment style and chronic pain burden emphasises the differences in threat perception between Secure and Insecure attachment styles. These findings add to a small body of work that offers valuable contributions to the fields of pain management and psychological health, proposing new avenues for understanding the social and psychological aspects of pain experiences and the development of more effective pain management strategies. For experimental pain, my study has provided important insights into the proportion of attachment styles, and the range of the attachment dimensions, for individuals who participate in experimental pain studies. These insights may be carried forward and improve future studies in the experimental pain field.

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APPENDIX 1

PART 1 – ETHICAL CLEARANCE

UNIVERSITY OF THE WITWATERSRAND, JOHANNESBURG

R49 Ms GE Stamp

HUMAN RESEARCH ETHICS COMMITTEE (MEDICAL)
CLEARANCE CERTIFICATE NO. M210449

NAME: (Principal Investigator)	Ms GE Stamp
DEPARTMENT:	School of Physiology Medical School University
PROJECT TITLE:	*The association between adult attachment style and pain, in a South African cohort*
DATE CONSIDERED:	2021/04/30
DECISION:	Approved unconditionally
CONDITIONS:	The approval of the Registrar is required to include Wits students as study paticipants <Nicoleen.Potgieter@wits.ac.za>
SUPERVISOR:	Drs A Wadley and S Iacovides
APPROVED BY:	Dr CB Penny, Chairperson, HREC (Medical)
DATE OF APPROVAL:	2021/07/22 (Revised)

This Clearance Certificate is valid for 5 years from the date of approval. An extension may be applied for.

DECLARATION OF INVESTIGATORS

To be completed in duplicate and **ONE COPY** returned to the Research Office secretariat on the 3rd floor, Phillip Tobias Building, Parktown, University of the Witwatersrand, Johannesburg.

I/we fully understand the conditions under which I am/we are authorized to carry out the above-mentioned research and I/we undertake to ensure compliance with these conditions. Should any departure be contemplated from the research protocol as approved, I/we undertake to submit details to the Committee. **I agree to submit a yearly progress report**. When a funder requires annual re-certification, the application date will be one year after the date when the study was initially reviewed. In this case, the study was initially reviewed in **April** and therefore reports and re-certification will be due in the month of **April** each year. Unreported changes to the study may invalidate the clearance given by the HREC (Medical).

Signature of Principal Investigator

23/07/2021
Date

APPENDIX 2

PART 2 – ETHICAL CLEARANCE

UNIVERSITY OF THE WITWATERSRAND, JOHANNESBURG

R49 Ms GE Stamp

HUMAN RESEARCH ETHICS COMMITTEE (MEDICAL)
CLEARANCE CERTIFICATE NO. M211003

NAME: (Principal Investigator) — Ms GE Stamp

DEPARTMENT: School of Physiology
Medical School
University

PROJECT TITLE: *The association between adult attachment style and pain perception in a South African cohort*

DATE CONSIDERED: 2021/10/29

DECISION: Approved unconditionally

CONDITIONS:

NOTE: If contact information regarding student study participants is required, please contact the Registrar's office - <Nicoleen.Potgieter@wits.ac.za>

SUPERVISOR: Drs S Iacovides and A Wadley

APPROVED BY: CB Penny
Dr CB Penny, Chairperson, HREC (Medical)

DATE OF APPROVAL: 2022/04/21

This Clearance Certificate is valid for 5 years from the date of approval. An extension may be applied for.

DECLARATION OF INVESTIGATORS

To be completed in duplicate and **ONE COPY** returned to the Research Office secretariat on the 3rd floor, Phillip Tobias Building, Parktown, University of the Witwatersrand, Johannesburg.

I/we fully understand the conditions under which I am/we are authorized to carry out the above-mentioned research and I/we undertake to ensure compliance with these conditions. Should any departure be contemplated from the research protocol as approved, I/we undertake to submit details to the Committee. **I agree to submit a yearly progress report**. When a funder requires annual re-certification, the application date will be one year after the date when the study was initially reviewed. In this case, the study was initially reviewed in **October** and therefore reports and re-certification will be due in the month of **October** each year. Unreported changes to the study may invalidate the clearance given by the HREC (Medical).

Signature of Principal Investigator

21/04/2022
Date

APPENDIX 3

SURVEY QUESTIONNAIRES

(This consent form and survey were completed electronically via REDCap)

Informed consent

Good day, my name is Gabriella Stamp and I am a PhD student in the School of Physiology at the University of the Witwatersrand. I am conducting a survey to determine if there is a relationship between adult attachment style and pain perception.

If you are at least 18 years old, grew up in South Africa and are currently living in South Africa, my supervisors and I invite you to participate in this survey.

It will take about ***10-15 minutes*** to complete.

There are multiple factors that affect having pain and the experience of that pain. Consequently, in addition to attachment style, there are questions about sleep, your mood, how you think about pain when you have it and about pain if you experience it regularly. Some of the symptoms of Covid-19 are similar to those of chronic pain (e.g. fatigue) and so we ask briefly if you have had Covid.

The results of the survey will provide invaluable information about adult attachment styles and pain perception in South Africa and may contribute to the development of improved treatments of pain.

Your participation in this study is completely voluntary and you may leave the survey at any point and without explanation. The data collected in this survey is completely confidential and your anonymity is guaranteed. All data collected will be used for scientific purposes only. All published data will be based on aggregated data only.

This study has been approved by the Human Research Ethic Committee (Medical) of the University of the Witwatersrand.

If you have any questions or concerns about the survey, please feel free to contact myself or my supervisors:

Gabriella Stamp
1604615@students.wits.ac.za

Dr Antonia Wadley
Antonia.wadley@wits.ac.za

Dr Stella Iacovides
Stella.iacovides@wits.ac.za

Do you want to participate in this study?

By clicking "yes" you consent to take part in the survey. You also consent to the use of your anonymous data in this study and future studies, should ethical clearance for subsequent studies be obtained.

Remember, you may leave the survey at any point should you wish to withdraw from participating. If you withdraw, all data you have already provided will be destroyed.

Yes / No

Demographic Information

Age

What is your age?

____

Area of Residence

Please select the province where you live.

Eastern Cape	
Free State	
Gauteng	
KwaZulu-Natal	
Limpopo	
Mpumalanga	
Northern Cape	
North West	
Western Cape	

Gender

What is your gender? Please select the applicable option.

Male	
Female	
Other	

Ethnicity

What is your race/ethnicity? Please select the applicable option.

Black	
White	
Indian	
Asian	
Hispanic	
Mixed race	
Other	

Language

What is your home language(s)? Please select the applicable option(s).

English	

Afrikaans	
Zulu	
Xhosa	
Venda	
Southern Sotho	
Northern Sotho	
Tswana	
Tsonga	
Swati	
Ndebele	
Other	

Education

What is your highest level of education? Please select the applicable option.

No schooling completed	
Nursery school	
Primary school (Grade 1-7)	
Some high school (Did not graduate matric)	
Completed high school (Graduated matric)	
Some university or college credit (no degree)	
Trade/technical/vocational training	
Tertiary degree (undergraduate)	
Tertiary degree (postgraduate)	

Annual Financial Income

What is your annual household financial income (combined income of any person(s) in the household contributing to the income of the household, including parents)? Please select the applicable option. (Statistics South Africa, 2011)

Low income (R1-R19 200)	
Middle income (R19 201-R307 200)	
High income (>R307 200)	

Marital Status

What is your marital status? Select the applicable option.

Single, never married	

Married or domestic partnership	
Separated	
Divorced	
Widowed	

Employment Status

What is your employment status? Select the applicable option(s).

A student	
Unemployed and looking for work	
Unemployed but not currently looking for work	
Employed part-time	
Employed full-time	
Self-employed	
Receiving a pension	
Receiving a grant	
Unable to work	

COVID-19 Information

COVID-19 Status

Please select the applicable option.

Have never tested positive for COVID-19	
Have tested positive for COVID-19	

COVID-19 Severity

How severe were/are your COVID-19 symptoms? Please select the applicable option.

Mild (No or mild symptoms but was able to function normally)	
Moderate (Symptoms required bed rest and made normal functioning difficult)	
Severe (Symptoms were so severe they required hospitalisation)	
Extremely Severe (Required some form of life support, e.g. a ventilator)	

Menstruation Information

Menstruation Regularity

Would you describe your menstrual cycle as regular?

Yes	
No	

I do not have a menstrual cycle (e.g. due to menopause, birth control or other)	

Menstruation Pain

Do you experience pain when menstruating? Please select the most applicable option.

Yes, mild pain	
Yes, moderate pain	
Yes, severe pain	
No, I do not experience pain while menstruating	

Duration of Menstruation Pain

For how long have you been experiencing menstruation pain? Please select the most applicable answer.

Less than 3 months	
3-12 month	
> 1 year	

Physiological Factors

Sleep Quality

How would you describe your quality of sleep over the past 6 months? Please select the most applicable option.

Very good	
Fairly good	
Fairly bad	
Very bad	

Sleep Regularity

Over the last 6 months, have you gone to sleep and woken up at the same time each day? Please select the most applicable option.

Mostly (5-7 days a week)	
Sometimes (2-4 days a week)	
Inconsistent bed and wake times	

Depression, Anxiety and Stress Scale – 21 (DASS21)

Please read each statement and circle a number 0, 1, 2 or 3 which indicates how much the statement applied to you over the past week. There are no right or wrong answers. Do not spend too much time on any statement.

The rating scale is as follows:

0 – Did not apply to me at all

1 – Applied to me to some degree, or some of the time

2 – Applied to me to a considerable degree or a good part of time

3 – Applied to me very much or most of the time

1 (s)	I found it hard to wind down	0	1	2	3
2 (a)	I was aware of dryness of my mouth	0	1	2	3
3 (d)	I couldn't seem to experience any positive feeling at all	0	1	2	3
4 (a)	I experienced breathing difficulty (e.g. excessively rapid breathing, breathlessness in the absence of physical exertion)	0	1	2	3
5 (d)	I found it difficult to work up the initiative to do things	0	1	2	3
6 (s)	I tended to over-react to situations	0	1	2	3
7 (a)	I experienced trembling (e.g. in the hands)	0	1	2	3
8 (s)	I felt that I was using a lot of nervous energy	0	1	2	3
9 (a)	I was worried about situations in which I might panic and make a fool of myself	0	1	2	3
10 (d)	I felt that I had nothing to look forward to	0	1	2	3
11 (s)	I found myself getting agitated	0	1	2	3
12 (s)	I found it difficult to relax	0	1	2	3
13 (d)	I felt down-hearted and blue	0	1	2	3
14 (s)	I was intolerant of anything that kept me from getting on with what I was doing	0	1	2	3
15 (a)	I felt I was close to panic	0	1	2	3
16 (d)	I was unable to become enthusiastic about anything	0	1	2	3
17 (d)	I felt I wasn't worth much as a person	0	1	2	3
18 (s)	I felt that I was rather touchy	0	1	2	3
19 (a)	I was aware of the action of my heart in the absence of physical exertion (e.g. sense of heart rate increase, heart missing a beat)	0	1	2	3
20 (a)	I felt scared without any good reason	0	1	2	3
21 (d)	I felt that life was meaningless	0	1	2	3

Pain Catastrophizing Scale (PCS)

Everyone experiences painful situations at some point in their lives. Such experiences may include headaches, tooth ache/pain, joint or muscle pain. People are often exposed to situations that may cause pain such as illness, injury, dental procedures or surgery.

We are interested in the types of thoughts and feelings that you have when you are in pain. Listed below are thirteen statements describing different thoughts and feelings that may be associated with pain. Using the following scale, please indicate the degree to which you have these thoughts and feelings when you are experiencing pain.

0 – Not at all **1** – To a slight degree **2** – To a moderate degree **3** – To a great degree **4** – All the time

When I'm in pain…

1. I worry all the time about when the pain will end. _____
2. I feel I can't go on. _____
3. It's terrible and I think it's never going to get any better. _____
4. It's awful and I feel that it overwhelms me. _____
5. I feel I can't stand it anymore. _____
6. I become afraid the pain will get worse. _____
7. I keep thinking of other painful events. _____
8. I anxiously want the pain to go away. _____
9. I can't seem to keep it out of my mind. _____
10. I keep thinking about how much it hurts. _____
11. I keep thinking about how badly I want the pain to stop. _____
12. There's nothing I can do to reduce the intensity of the pain. _____
13. I wonder whether something serious may happen. _____

*Total*_______

Experience in Close Relationships – Relationship Structure (ECR-RS)

A. Please answer the following questions about your mother or a mother-like figure.

	Strongly Disagree	Disagree	Somewhat Disagree	Neither Agree nor Disagree	Somewhat Agree	Agree	Strongly Agree
It helps to turn to this person in times of need.							
I usually discuss my problems and concerns with this person.							
I talk things over with this person.							
I find it easy to depend on this person.							
I don't feel comfortable opening up to this person.							
I prefer not to show this person how I feel deep down.							
I often worry that this							

person doesn't really care for me.							
I'm afraid that this person may abandon me.							
I worry that this person won't care about me as much as I care about him or her.							

B. Please answer the following questions about your father or a father-like figure.

	Strongly Disagree	Disagree	Somewhat Disagree	Neither Agree nor Disagree	Somewhat Agree	Agree	Strongly Agree
It helps to turn to this person in times of need.							
I usually discuss my problems and concerns with this person.							
I talk things over with this person.							

I find it easy to depend on this person.							
I don't feel comfortable opening up to this person.							
I prefer not to show this person how I feel deep down.							
I often worry that this person doesn't really care for me.							
I'm afraid that this person may abandon me.							
I worry that this person won't care about me as much as I care about him or her.							

C. Please answer the following questions about your dating or marital partner. Note: If you are not currently in a dating or marital relationship with someone, answer these questions with respect to a former partner or a relationship that you would like to have with someone.

	Strongly Disagree	Disagree	Somewhat Disagree	Neither Agree nor Disagree	Somewhat Agree	Agree	Strongly Agree
It helps to turn to this person in times of need.							
I usually discuss my problems and concerns with this person.							
I talk things over with this person.							
I find it easy to depend on this person.							
I don't feel comfortable opening up to this person.							
I prefer not to show this person how I feel deep down.							
I often worry that this person doesn't really care for me.							

I’m afraid that this person may abandon me.							
I worry that this person won't care about me as much as I care about him or her.							

D. Please answer the following questions about your best friend.

	Strongly Disagree	Disagree	Somewhat Disagree	Neither Agree nor Disagree	Somewhat Agree	Agree	Strongly Agree
It helps to turn to this person in times of need.							
I usually discuss my problems and concerns with this person.							
I talk things over with this person.							

I find it easy to depend on this person.							
I don't feel comfortable opening up to this person.							
I prefer not to show this person how I feel deep down.							
I often worry that this person doesn't really care for me.							
I’m afraid that this person may abandon me.							
I worry that this person won't care about me as much as I care about him or her.							

General pain information

Have you had pain most days for the last month?

Yes No

Have you had pain most days for the last three months?

Yes No

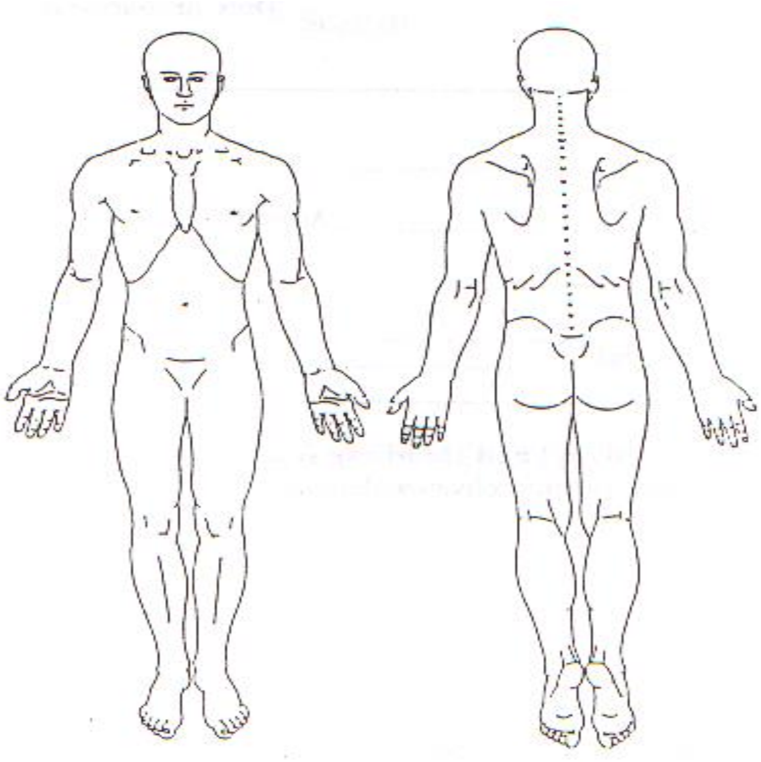
Brief Pain Inventory – short form (BPI-sf)

1. Throughout our lives, most of us have had pain from time to time (such as minor headaches, sprains, and toothaches).

   Have you had pain other than these everyday kinds of pain during the last week?

   Yes No

2. On the diagram, shade in the areas where you feel pain. Put an **X** on the area that hurts the most.



3. Please rate your pain by circling the one number that best describes your pain at its ***worst*** in the last week.

0	1	2	3	4	5	6	7	8	9	10
No pain										Pain as bad as

4. Please rate your pain by circling the one number that best describes your pain at its ***least*** in the last week.

0 1 2 3 4 5 6 7 8 9 10

No pain

Pain as bad as you can imagine

5. Please rate your pain by circling the one number that best describes your ***average*** pain in the last week.

0 1 2 3 4 5 6 7 8 9 10

No pain

Pain as bad as you can imagine

6. Please rate your pain by circling the one number that tells how much pain you have ***right now.***

0 1 2 3 4 5 6 7 8 9 10

No pain

Pain as bad as

7. What treatments or medications are you receiving for your pain?

8. In the last 24 hours, how much relief have pain treatments or medications provided? Please mark the box below the percentage that most shows how much relief you have received.

0% 10% 20% 30% 40% 50% 60% 70% 80% 90% 100%

no relief complete relief

9. Circle the one number that describes how much, during the past week, **pain** has ***interfered with*** your:

A. *General Activity*

0 1 2 3 4 5 6 7 8 9 10

Does not interfere

Completely interferes

B. Mood

0 1 2 3 4 5 6 7 8 9 10

Does not interfere

Completely interferes

C. ***Walking Ability***

0 1 2 3 4 5 6 7 8 9 10

Does not interfere | Completely interferes

D. ***Normal Work*** (includes both work outside the home and housework)

0 1 2 3 4 5 6 7 8 9 10

Does not interfere | Completely interferes

E. ***Relations with other people***

0 1 2 3 4 5 6 7 8 9 10

Does not interfere | Completely interferes

F. ***Sleep***

0 1 2 3 4 5 6 7 8 9 10

Does not interfere | Completely interferes

G. ***Enjoyment of life***

0 1 2 3 4 5 6 7 8 9 10

Does not interfere | Completely interferes

Would you like to help us further?

If you are female, live in Johannesburg and would be willing to travel to the University of the Witwatersrand, would you like to participate in the next phase of our study?

Yes / No

If “Yes”, then please leave your email address so that we can contact you with more information.

Would you like to hear the results of this study?

Yes / No

If “Yes”, then please leave your email address so that we can contact you with the published results.

APPENDIX 4

EXPERIMENTER MANNER SCRIPT

Neutral Experimenter Script and Guidelines

General mannerism guidelines

- Act professional but not friendly or aloof.
- When asked questions, answer politely but with a professional detachment.
- Wear lab coat buttoned up.

Greeting the participant

- Introduce yourself as Gabriella Stamp, a PhD student.
- Smile politely when you greet the participant.
- Do not engage in any small talk (in other words, do not comment on the weather or compliment her clothes).

The experiment

- Explain the experiment in a professional manner. In other word, you will talk as if you are explaining a process in a business meeting – concise but not aloof.
- When asking them to fill in the questionnaire on the computer, be polite but not friendly.
- When conducting the experiment, do not make small talk. Should the participant try to make conversation, reply politely but make no attempt to continue the conversation unnecessarily.
- If the participant makes remarks about the experiment being painful, acknowledge them and remind them that it will not cause any tissue damage. Do not offer any sympathy, but also do not brush off their comments.

The experimenter manner check

- Politely ask the participant to fill out the post-experimental pain procedure questionnaire. Explain to them that the first question pertains to the manner of the experimenter. Ask them to please answer the question honestly and not what they think you want them to answer.

Once the participant has filled out the experimenter manner check and completed the rest of the post-experimental pain procedure questionnaire, she will be thanked and told that the experiment is over.

Ask the participant if they have any questions and check that the pain from the thermode and cold water bath has subsided. Thank her for participating and give her the R250 travel compensation.

APPENDIX 5

EXPERIMENTAL PAIN PROCEDURE INFORMATION SHEET

UNIVERSITY OF THE WITWATERSRAND, JOHANNESBURG

School of Physiology, Faculty of Health Sciences
Medical School, 7 York Road, Parktown 2193, South Africa

November 2022

Participant information sheet

Project: ***The association between adult attachment stye and pain in a South African cohort***

Good day,

My name is Gabriella Stamp, and I am a PhD student in the School of Physiology at the University of the Witwatersrand. My supervisors and I are conducting a study to see if there is an association between pain sensitivity and adult attachment style. We would like to invite you to take part.

What is involved in the study?

You will be asked to travel to the University of the Witwatersrand Health Science campus to take part in the experiment.

You will be asked to fill out a questionnaire and to be involved in an experimental procedure called conditioned pain modulation.

What does the questionnaire ask?

The questionnaire will assess whether you have increased sensitisation to pain. The questionnaire will be filled out anonymously on a computer set up in a lab in the School of Physiology. The questionnaire should take about 5 minutes to complete.

What does the conditioned pain modulation experiment entail?

The conditioned pain modulation procedure has three phases. In the first phase, a thermode will be strapped to your left leg and your arm will rest on top of the warm part of the. The temperature of the thermode will be gradually increased until it reaches a maximum of 52°C (It is very hot, like a hot bath/sauna, but will not harm you). You will be asked to click a button when the temperature becomes uncomfortable, and you click again when the heat is as much as you can tolerate. We will repeat this three times and then calculate a temperature that you will rate at about 6/10 (0 being no pain or discomfort and 10 being your worst pain).

In the second phase, the thermode will be place on your right leg with the warm part facing up. Your right arm will rest on the thermode. The temperature of the thermode will increase gradually until the temperature we calculated from the first phase is reached. This temperature will be at an intensity rating of about 6/10. The thermode will remain at this temperature for two minutes, during which time you will verbally rate your pain every 10 seconds. A rating of 0 = No pain and 10 = worst pain imaginable.

The third phase will occur five minutes after the second phase. In the third phase, the entire process of the second phase will be repeated, but now your other hand will be submerged in icy cold water (7°C). In other words, your left hand will be submerged in the cold water while the thermode is hot on your right arm. Again, you will be asked to rate the discomfort from the thermode continuously over the course of two minutes. After two minutes, you will be asked to remove your hand from the water and verbally rate the pain in that hand on a scale from

0-10, as mentioned above.

How long will it take?

The whole process should take about 1 hour from when you arrive at the School of Physiology lab until the end the procedure.

What are the risks of taking part?

The only risk is that you will likely feel discomfort or even pain during the procedure and it could last for a few minutes afterwards. The procedures are designed to feel intense but the temperatures we use (both hot and cold) will not cause any tissue damage. You are also allowed to stop the experiment at any point.

How will I benefit by taking part?

You will not benefit directly from the study. You will, however, receive R250 compensation for travelling to the University of the Witwatersrand Health Science campus to partake in our study.

Can I leave the study?

You are free to leave the study at any time. There are no repercussions for you doing so. You will also not be required to provide a reason should you choose to leave the study.

Should you decide to leave the study, you may provide consent for your data that is already collected to be used in the study and future studies going forward (where ethical clearance is obtained) or you may choose to withdraw consent, in which case data collected from you will be destroyed.

What information will be gathered and who will see it?

We will collect your, questionnaire, and conditioned pain modulation data. Only the members of the study team will know your name as they will organise when you come in for the experiments. Once both your experiments are complete, your data will be identified only by a study number and not your name so your data will be anonymous.

After the study, only aggregated data of the whole group will be used for analysis and publication and so your responses will not be revealed.

Who can I contact about this research?

You may contact myself (Gabriella Stamp) or my two supervisors, Dr Antonia Wadley and Dr Stella Iacovides, at any time to chat about the study or if you would like to receive information about our findings. Here are our contact details:

UNIVERSITY OF THE WITWATERSRAND, JOHANNESBURG

School of Physiology, Faculty of Health Sciences
Medical School, 7 York Road, Parktown 2193, South Africa

Gabriella Stamp
1604615@students.wits.ac.za
0718791849

Dr Antonia Wadley
Antonia.wadley@wits.ac.za
Room 7M14
011 717 2163

Dr Stella Iacovides
Stella.iacovides@wits.ac.za
Room 7M12
011 717 2265

This study has been approved by the Human Research Ethics Committee (Medical) of the University of the Witwatersrand, Johannesburg. A principal function of this Committee is to safeguard the rights and dignity of all human subjects who agree to participate in a research project and the integrity of the research.

If you have any concern over the way the study is being conducted, please contact the Chairperson of this Committee who is Professor Clement Penny, who may be contacted on telephone number 011 717 2301, or by e-mail on Clement.Penny@wits.ac.za.

The telephone numbers for the Committee secretariat are 011 717 2700/1234 and the e-mail addresses are Zanele.Ndlovu@wits.ac.za and Rhulani.Mukansi@wits.ac.za.

Thank you very much for considering taking part in the study.

Yours sincerely,

Gabriella Stamp

APPENDIX 6

EXPERIMENTAL PAIN PROCEDURE CONSENT FORM

(This form was completed electronically via REDCap)

Informed consent

Project: ***The association between adult attachment style and pain in a South African cohort***

1. I have been given a Participant Information Sheet which explains the nature and processes involved in this study, which is attached hereto.
2. I was given time to read it, or had it read to me.
3. I was given time to ask any questions I wanted to and found any answers given to me to be reasonable and satisfactory.
4. I believe I fully understand why the study is being conducted and what the intended outcomes will be.
5. I understand that participation will require me to travel to the University of Witwatersrand Health Science campus and spend about 1 hour being involved in the study.
6. I understand that there will be no immediate benefit to me, but I will receive travel compensation of R250, should I agree to participate.
7. I understand that, even if I initially consent to take part in the study, I may subsequently withdraw at any time and would not be required to give any reasons; if that happened, any data collected about me for the purposes of the study would immediately be destroyed, unless I give consent for it to be retained
8. I have been given a range of contact details, listed below. If I require further information or become concerned about any aspect of this study, I am free to speak to any of these contacts.

Contact details:

Gabriella Stamp, Principal Investigator, cell phone no. 0718791849, or by e-mail at

1604615@students.wits.ac.za

Antonia Wadley, telephone no. 011 717 2163 or 078 802 8182, or by e-mail at

antonia.wadley@wits.ac.za

Professor CB Penny, Chairperson of the Human Research Ethics Committee (Medical) at the University of Witwatersrand, on telephone no. 011 717 2301, or by e-mail at Clement.Penny@wits.ac.za.
Ms. Z Ndlovu or Mr Rhulani Mkansi, Committee Secretariat, telephone nos.: 011 717 2700 or 1234, or by e-mail at: Zanele.Ndlovu@wits.ac.za or Rhulani.Mkansi@wits.ac.za

Name of Participant: ________________________________

Date: ________________________________

Place: ________________________________

Signature or mark ________________________________

Witnessed by:

Name of Witness: ________________________________

Signature: ________________________________

Date: ________________________________

APPENDIX 7

PRE-EXPERIMENTAL PAIN PROCEDURE QUESTIONNAIRES

(This questionnaires were completed electronically via REDCap)

Current pain status

Are you currently in pain? *(Only able to select one option).*

No	
Yes	

Have you taken any pain medication in the last 6 hours? *(Only able to select one option).*

No	
Yes	

Menstrual information

To the best of your knowledge, are you pregnant? *(Only able to select one option).*

No	
Yes	

If you answered "no" to the previous question, do you experience a menstrual cycle? *(Only able to select one option).*

No	
Yes	

If you answered "yes" to the previous question, are you currently menstruating? *(Only able to select one option).*

No	
Yes	

If you answered "yes" to the previous question, what date did your last menstruation start?

____

If you answered "no" to the previous question, to the best of your knowledge, what date did your last menstruation start?

____

APPENDIX 8

POST-EXPERIMENTAL PAIN PROCEDURE QUESTIONNAIRE

(This questionnaire was completed electronically via REDCap)

Experimenter Manner

The manner of the experimenter is important for our study. Please be completely honest and select whether you felt the experimenter was friendly, neutral/professional, or rude/aloof. *(Only able to select one option).*

Friendly	
Neutral/Professional	
Rude/Aloof	

Additional information and comments

Regardless of the season, are your hands and feet typically cold or warm? *(Only able to select one option).*

Cold	
Warm	
Neither	
I don't know	

How would you describe the pain from the thermode? Mention any sensations, discomfort, kinds of pain and/or emotions evoked by the pain.

____

____

Did you find the pain from the thermode threatening? *(Only able to select one option).*

No	
Yes	

How would you describe the pain from the cold water? Mention any sensations, discomfort, kinds of pain and/or emotions evoked by the pain.

____

____

Did you find the pain from the cold water threatening? *(Only able to select one option).*

No	
Yes	

Thank you

Would you be interested in hearing our results? *(Only able to select one option).*

No	
Yes	

If “yes”, please enter your email address