The Biopsychosocial Factors Associated With Pain In People With Spinal Cord Injury

Margaret Patricia Tilley

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Abstract

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Background: It is estimated that over 62% of people with a spinal cord injury (SCI) experience chronic pain, (Ullrich, Jensen, Loesser & Cardenas, 2007). Much research has demonstrated that a variety of biopsychosocial factors can impact on pain outcomes (Tran, Dorstyn & Burke, 2016) and, consequently on adjustment to injury. It is also well established that cognitive appraisal of SCI impacts on psychological adjustment during rehabilitation (Eaton, Jones & Duff, 2018). SCI pain is unusually resistant to standard pain management programmes (Perry, Nicholas & Middleton, 2010). However, the development of a tailored programme requires a profile of the biological, psychological, and social characteristics of chronic pain sufferers with SCI, but the existing knowledge base is fragmented. This study aimed to investigate how biopsychosocial factors interact to impact on pain-related outcomes for people with SCI.

Method: A longitudinal, multiple assessment-point design was used with 60 spinal cord injured in-patients at the NSIC, Stoke Mandeville. Participants were asked to complete a set of two pain and six psychological assessments at three different time points over a nine-month period, and to provide salivary samples on each occasion to assess concentration levels of cortisol. Additionally, a cross-sectional study using the same questionnaires and cortisol sampling was undertaken with 47 out-patients, who had been discharged a minimum of two years previously from the NSIC. Cohen's (2009) power primer was used to calculate sample size. Independent *t*-tests measured differences between in-patient and out-patient groups on each questionnaire. Multiple regression was used to determine which biopsychosocial factors have greater predictive power in accounting for a range of functional, affective and sensory pain outcomes, highlighting how variables may individually and in combination influence the pain experience.

Repeated measures ANOVAs were used to assess how the data changed over time and each measure was additionally correlated with time since injury. Additional exploratory analyses were undertaken to see whether pain catastrophising, appraisal of injury and pain acceptance mediated the effects of the other biopsychosocial variables on the pain outcomes. Lastly, multiple regressions explored whether the psychosocial variables predicted the way in which the injury was appraised.

Results: Out-patients appraised their injury more negatively (p = .04) and had lower determined resilience (p = .05) than in-patients at time one. They also demonstrated less pain acceptance (p = .04) and received fewer solicitous responses from a significant other person (p = .01). In-patients at time three had higher depression scores than out-patients (p = .006). In the multiple regression analyses, negative psychological variables predicted pain intensity (p = .002-.005), interference from pain (p = .001), and pain-related distress (p = .001). Positive psychological variables did not predict pain intensity but did predict pain interference (p = .029 - .071) and distress (p <.001). The way a significant other responded to the individual in pain did not predict pain intensity but did predict life interference (p = .001) and distress (p = .018 - .049). Cortisol did not predict any of the pain outcomes directly. Of all the variables, cortisol concentration was only significantly related to pain catastrophising (p = .008). The in-patient longitudinal analysis showed that over the three time points determined resilience decreased (p <.001), and depression scores increased (p = .025). The magnification sub scale of pain catastrophizing also increased between the first and second time point (p = .021). Time since injury was positively correlated with mental defeat (p = .047) and the helplessness sub scale of pain catastrophizing (p = .010), and negatively correlated with cortisol concentration levels (p = .001). In the mediation analyses, pain catastrophizing and appraisal of injury mediated the effects of most of the biopsychosocial variables on a wide range of pain outcomes. Pain catastrophizing was most influential on sensory and functional pain outcomes, and injury appraisal had greater effects on affective and functional outcomes. Pain acceptance was not influential as a mediating variable. In the final multiple regression analyses, the psychosocial variables were entered into regression models to see if they would predict the way the

spinal injury was appraised. The psychological variables model (catastrophizing, acceptance, perceived stress, anxiety and mental defeat) predicted catastrophic negativity (p <.001) and determined resilience (p <.001). The way a significant person responded to the individual in pain did not predict catastrophic negativity with regard to injury appraisal but did predict determined resilience (p = .001).

Conclusion: The results of this study clearly indicate that biopsychosocial variables combine and interact to affect the consequences of pain for people with spinal cord injury. Pain treatment programmes that fail to take account of each of the components of the biopsychosocial model will not be addressing all of the factors associated with the pain experience, and this will have a negative impact for those in pain. This is especially concerning as the study found that psychosocial variables worsen on transition to the community. Appraisal of injury and pain catastrophizing are particularly influential, both as predictors and mediators, so focusing on these factors in pain management could improve pain outcomes and injury adjustment for people with spinal cord injury.

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Abbreviations

ACT	Acceptance and Commitment Therapy
ACTH	Adrenocorticotropic hormone
ADAPSS	Appraisal of Disability Primary and Secondary Scale
ANS	Autonomic Nervous System
APA	American Psychological Association
ASIA	American Spinal Injuries Association
AVP	Arginine Vasopressin
Aβ	A Beta
Aδ	A Delta
BA 8	Brodmann's Area 8
BLA	Basolateral Amygdala
cAMP	Cyclic adenosine monophosphate pathway
CAR	CAR
CBT	Cognitive Behaviour Therapy
CCM	Communal Coping Model
CeA	Central nucleus of the amygdala
CNS	Central nervous system
CPAQ	Chronic Pain Acceptance Questionnaire
CRF	Corticotropin-releasing factor
CRFR1	Corticotropin-releasing factor type 1 receptors
dACC	Dorsal anterior cingulate cortex
DAG	Diacylglycerol
DLPT	Dorsolateral pontine tegmentum
DNIC	Diffuse noxious inhibitory control
DRt	Dorsal reticular nucleus
FA	Fear Avoidance Model
fMRI	Functional magnetic resonance imaging
GAD	Generalised Anxiety Disorder
HADS	Hospital Anxiety and Depression Scale
HPA	Hypothalamus-Pituitary-Adrenal

IASP	International Association for the Study of Pain
IDS	Involuntary defeat strategy
IP3	Inositol triphosphate
ISCIP	International Spinal Cord Injury Pain
ISNCSCI	International Standards for Neurological Classification of Spinal Cord Injury
LA	Lateral amygdala
LANSS	Leeds Assessment of Neuropathic Symptoms and Signs
LC	Locus Coeruleus
MC2-R	Melanocortin type 2 receptor
MDD	Major Depressive Disorder
MPI-SCI	Multidimensional Pain Inventory – Spinal Cord Injury
MPIA	Multidimensional Pain Inventory Section A
MPIB	Multidimensional Pain Inventory Section B
MPIC	Multidimensional Pain Inventory Section C
MPICa	Multidimensional Pain Inventory Section C – activity level
MPICb	Multidimensional Pain Inventory Section C – activities reduced by pain
MPM	Misdirected Problem Solving Model
NFR	Nociceptive flexion reflex
NLI	Neurological level of injury
NRM	Nucleus Raphe Magnus
NRS	Numerical rating scale
NSAID	Non-steroidal anti-inflammatory drugs
NSIC	National Spinal Injuries Centre
PAG	Periaqueductal Grey
PCS	Pain Catastrophizing Scale
PSPS	Pain Self-Perception Scale
PSS	Perceived Stress Scale
PTSD	Post-Traumatic Stress Disorder
PVN	Paraventricular nuclei of the hypothalamus

RVM	Rostral ventromedial medulla
SCI	Spinal cord injury
SIA	Spinal Injuries Association
Spinal region C	Cervical
Spinal region L	Lumba
Spinal region S	Sacral
Spinal region T	Thoracic
TMD	Temporomandibular Disorder
TNS	Tumor necrosis factor
TS-NFR	Temporal summation - Nociceptive flexion reflex
TSCI	Traumatic spinal cord injury
VLPFC	Ventrolateral prefrontal cortex
VMPFC	Ventromedial prefrontal cortex

Table of Contents

List of Figures

List of Tables

Declaration of Originality

I hereby declare that my thesis entitled The Biopsychosocial Factors Associated With Pain in People With Spinal Cord Injury is the result of my own work and includes nothing which is the outcome of work done in collaboration except as declared in the Preface and specified in the text, and is not substantially the same as any that I have submitted, or, is concurrently submitted for a degree or diploma or other qualification at the University of Buckingham or any other University or similar institution except as declared in the Preface and specified in the text. I further state that no substantial part of my thesis has already been submitted, or is concurrently submitted for any such degree, diploma, or other qualification at the University of Buckingham or any other University or similar institution except as declared in the Preface and specified in the text.

Signature: Date:

2 Introduction

Pain is a problem for many people with a spinal cord injury (SCI). The purpose of this thesis is to contribute to the knowledge base by exploring the interactions between a range of variables and the impact they have on pain and its consequences. Two key perspectives have influenced, guided and inspired the implementation and design of this research: the Biopsychosocial Model of Health and Illness (Engel, 1977) and the Foundational Principles of Rehabilitation Psychology (Wright, 1983).

Pain research has traditionally concentrated on the biomedical model, focusing on the sensory aspects of pain and its neurological mechanisms (Gatchel, Peng, Peters, Fuchs & Turk, 2007). However, since Engel (1977) first introduced the biopsychosocial model of health, research into pain conditions has included a much wider range of contributing variables. The biopsychosocial model perceives illnesses, such as pain, as resulting from the complex and dynamic interaction of biological, psychological and social factors (Engel, 1977). These factors combine to modulate the experience of pain and subsequent degree of disability, which is unique to each individual. This model is now generally acknowledged to be the most heuristic perspective regarding pain and its treatment (Gatchel, et al., 2007). From this has stemmed the distinction between nociception and pain. Nociception is understood as being the sensory stimulation of pain receptors (nociceptors), and the conveyance of these pain messages to the brain. Pain, on the other hand, involves the perception of the physical sensation, which is influenced, for example, by psychological status, expectation, prior pain experiences, and social influences (Gatchel et al., 2007). This is conceptualised graphically below in Figure 1 where the complex interrelationships between the biological mechanisms, cognitions and the social environment are clearly displayed.

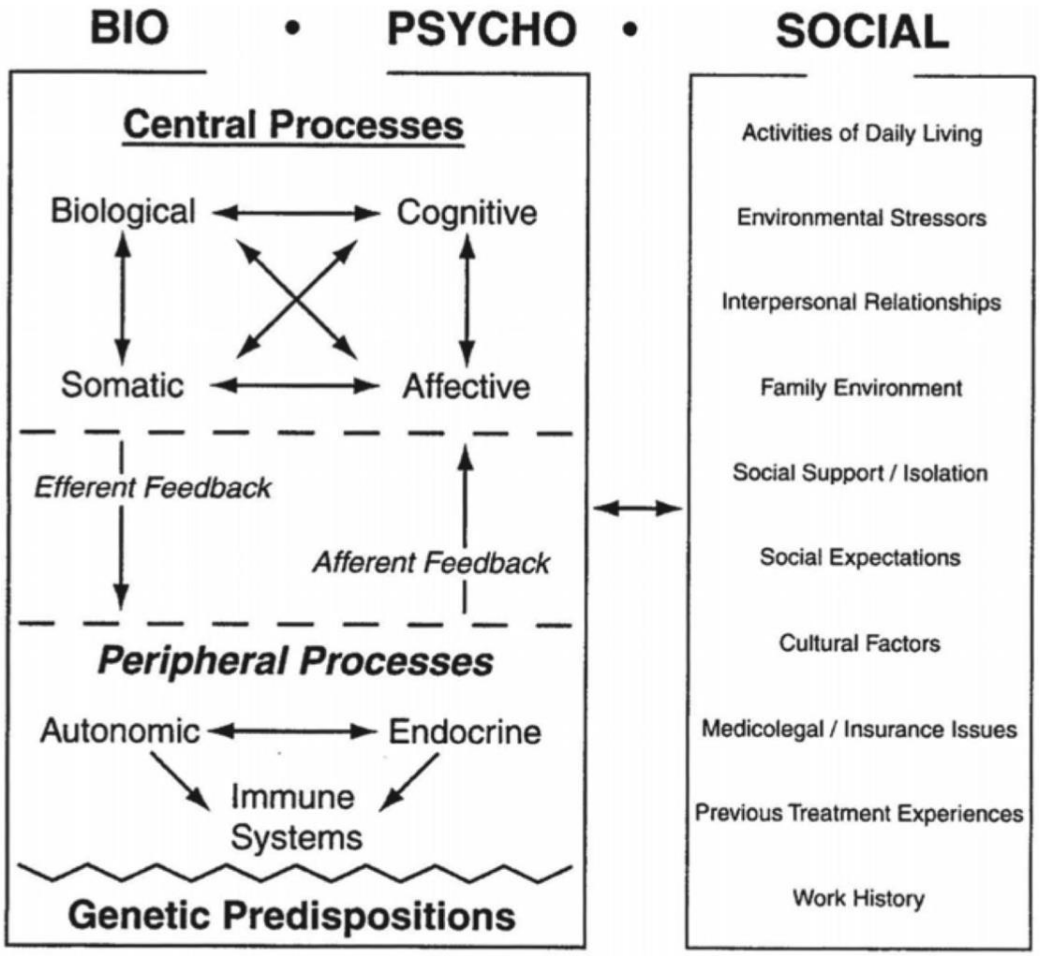

Figure 1 A conceptual model of the biopsychosocial interactive processes involved in health and illness. From "The biopsychosocial approach to chronic pain: Scientific advances and future directions," by R. J. Gatchel, Y. B. Peng, M. L. Peters, P. N. Fuchs, & D. C. Turk, 2004, *Psychological Bulletin, 133*, p. 583. Copyright 2007 by the American Psychological Association.

Despite the apparent dominance of the biopsychosocial model in recent years, and despite practice guidelines generally recommending this approach for pain management, the biomedical model continues to be more influential (Schmidt, 2016). This is particularly problematic where spinal cord injury is concerned because none of the current pharmacological pain treatments consistently relieve pain (Widerström-Noga, Finnerup, & Siddall, 2009). This thesis, therefore, is grounded in the biopsychosocial model. It has been said that studies claiming to be 'biopsychosocial' focus mostly on psychosocial factors, ignoring the biological aspects (Pincus et al., 2013). In response, this

thesis includes a focus on all three elements of the model, aiming to understand the complexity and variability in chronic pain (Edwards, Dworkin, Sullivan, Turk, & Wasan, 2016).

The second key influence for this thesis comes from the six Foundational Principles in rehabilitation psychology (Wright, 1983). These can be seen in Table 1 below. The person-environment relation describes how the individual with the spinal cord injury should not be defined by their injury, and situational factors need be considered rather than just the dispositional ones when explaining an individual's behaviour. This is associated with the second principle, the insider-outsider distinction, which explains how people assume that living life with a spinal cord injury is a very negative experience. People without a spinal cord injury tend to adopt a far more pessimistic view about what life would be like than that which is actually experienced. In one study, only 18% of staff in an emergency room thought they would be glad to be alive following SCI compared to 92% of actual spinal-cord injured patients (Gerhart, Koziol-McLain, Lowenstein & Whiteneck, 1994). These results have been replicated more recently and with a sample from the general population, where it was found that able-bodied participants had a far more negative view of how they would adapt and cope with spinal cord injury than those with an injury (Morris, Swiller-Vosnos, Dusold & Woodworth, 2013). This is crucial as people's attitudes can affect the way in which resources are allocated, make it more or less likely they will employ someone with a spinal cord injury and influence their likelihood of forming a social relationship with a spinal cord injured person (Morris, et al., 2013). It may also be important in the early stages of rehabilitation, as peoples prior assumptions about living life with spinal cord injury are likely to be quite pessimistic. Letting them know that living successfully with SCI is quite possible could provide much needed hope (Morris, et al., 2013).

Principle	Definition
The Person–Environment Relation	Attributions about people with disabilities tend to focus on presumed dispositional rather than available situational characteristics. Environmental constraints usually matter more than personality factors to living with a disability.
The Insider–Outsider Distinction	People with disabilities (*insiders*) know what life with a chronic condition is like (e.g., sometimes challenging but usually manageable) whereas casual observers (*outsiders*) who lack relevant experience presume that disability is defining, all encompassing, and decidedly negative.
Adjustment to Disability	Coping with a disability or chronic illness is an ongoing dynamic process, one dependent on making constructive changes to the social and the physical environment.
Psychosocial Assets	People with disabilities possess or can acquire personal or psychological qualities that can ameliorate challenges posed by disability and also enrich daily living.
Self-Perception of Bodily States	Experience of bodily states (e.g., pain, fatigue, distress) is based on people's perceptions of the phenomena, not exclusively the actual sensations. Changing attitudes, expectations, or environmental conditions can constructively alter perceptions.
Human Dignity	Regardless of the source or severity of a disability or chronic health condition, all people deserve respect, encouragement, and to be treated with dignity.

Note: From "The Foundation Principles as psychological lodestars: Theoretical inspiration and empirical direction in rehabilitation psychology" by D. S. Dunn, D. M. Ehde, and S. T. Wegener, 2016, *Rehabilitation Psychology, 61*(1), p. 2.

The third Foundational Principle recognises that there is a necessary process of adaptation to the spinal cord injury, which if successful, will result in adjustment. Various factors can influence the success of adaptation, as identified in the next two principles, and some individuals will adapt and adjust better than others. The principle of psychosocial assets recognises that people possess and/or can develop qualities, such as resilience for example, that can help them to adapt to their injury. It is important therefore, not to simply focus on negative characteristics, but to try to uncover the strengths that people possess (Wright, 1983). This helps people to focus on what they have and how this can help them to achieve their goals in the future (Dunn, Ehde, & Wegener, 2016). The fifth principle refers to the idea that the way people respond to bodily states, such as pain, results from their perceptions rather than the actual sensation. Perceptions can be influenced by various top-down processes, for example, expectations and prior learning (Dunn et al., 2016). This implies, however, that interventions could improve perceptions so that they are more helpful to the individual, without negating the validity of the original experience. Lastly, the principle of human dignity states that regardless of the severity of the disability, all people deserve to be treated with respect and dignity. Wright (1987, p. 12) concurred with this, saying “An essential core-concept of human dignity is that a person is not an object, not a thing”.

The Foundational Principles have been less influential in the past few decades, but have now come to the fore again. In their recent paper Dunn et al. (2016) refer to them as lodestars, something that can guide or inspire a group of people. Their suggestion is that the Foundational Principles are just as relevant today as they originally were, and that they can and should guide both research and practice. Additionally, the Foundational Principles were the focus of a workshop at the European Spinal Psychologists Association meeting (Rohe, 2019), ensuring that they continue to have prominence with practitioners and researchers alike. The study itself was designed using input from people with a spinal cord injury to ensure their voice was heard and their recommendations adhered to (principles one and two). Outcomes of pain associated with adjustment were included, as well as the sensory and affective

consequences (principle three). Both negative and positive psychological variables were measured so that strengths, as well as difficulties, could be acknowledged (principle four). Questionnaires that measured individuals' perception of their pain were included, alongside the sensory measure of pain severity (principle five). Lastly, people were treated with dignity and respect throughout the data collection, with awareness of both their physical and emotional needs remaining paramount (principle six). Therefore, as well as being grounded in the biopsychosocial model, this thesis has attempted to keep all six of the principles in mind during the design and implementation of this research.

3 Chapter 1 - Spinal Cord Injuries

The spinal cord is a bundle of nerves that runs from the brain through the spinal column. The spinal column is segmented into four sections; the cervical, thoracic, lumbar and sacral sections. As shown in Figure 2, the spinal cord consists of 31 pairs of nerve roots, corresponding with these sections, which carry messages to and from the central nervous system (the brain) via the peripheral nervous system. There are eight pairs of cervical nerves (C1 - C8) concerned with internal control functions, such as heart rate and respiration, and with movement in the upper limbs. The 12 pairs of thoracic nerves (T1 - T12) control body temperature and the trunk of the body. Lower limb movement is controlled by five pairs of lumbar nerves (L1 - L5) and bladder, bowel and sexual function is managed by five pairs of sacral nerves (S1 - S5). Lastly, one pair of coccygeal nerves innervates the skin over the coccyx and the levator ani and coccygeus muscles (the pelvic floor muscles). The spinal cord itself ends at the Conus Medullaris between the L1 and L2 regions. Continuing on from there, a collection of nerve roots called the Cauda Equina fan out to the lumbar, sacral and coccyx regions (see Figure 2).

The Back-Up Trust (2018) originally estimated that there were over 40,000 people living with a spinal cord injury (SCI) in the United Kingdom with over 1,000 people becoming newly injured every year. More recently, they along with The Spinal Injuries Association (SIA) and Aspire (three leading spinal injuries charities) have suggested that these figures are much higher. They report that new data from the National Health Service suggest that people living with spinal cord injury number closer to 50,000, and that each year 2,500 people become newly injured (Spinal Injuries Association, 2019). A spinal cord injury results from a lesion to any part of the spinal cord, conus medullaris or the cauda equina. Movement immediately after injury can result in further damage, but ongoing exacerbation of the injury is also common and is contributed to by complex inflammatory processes reducing oxygen and blood flow to the damaged area (Okada, 2016).

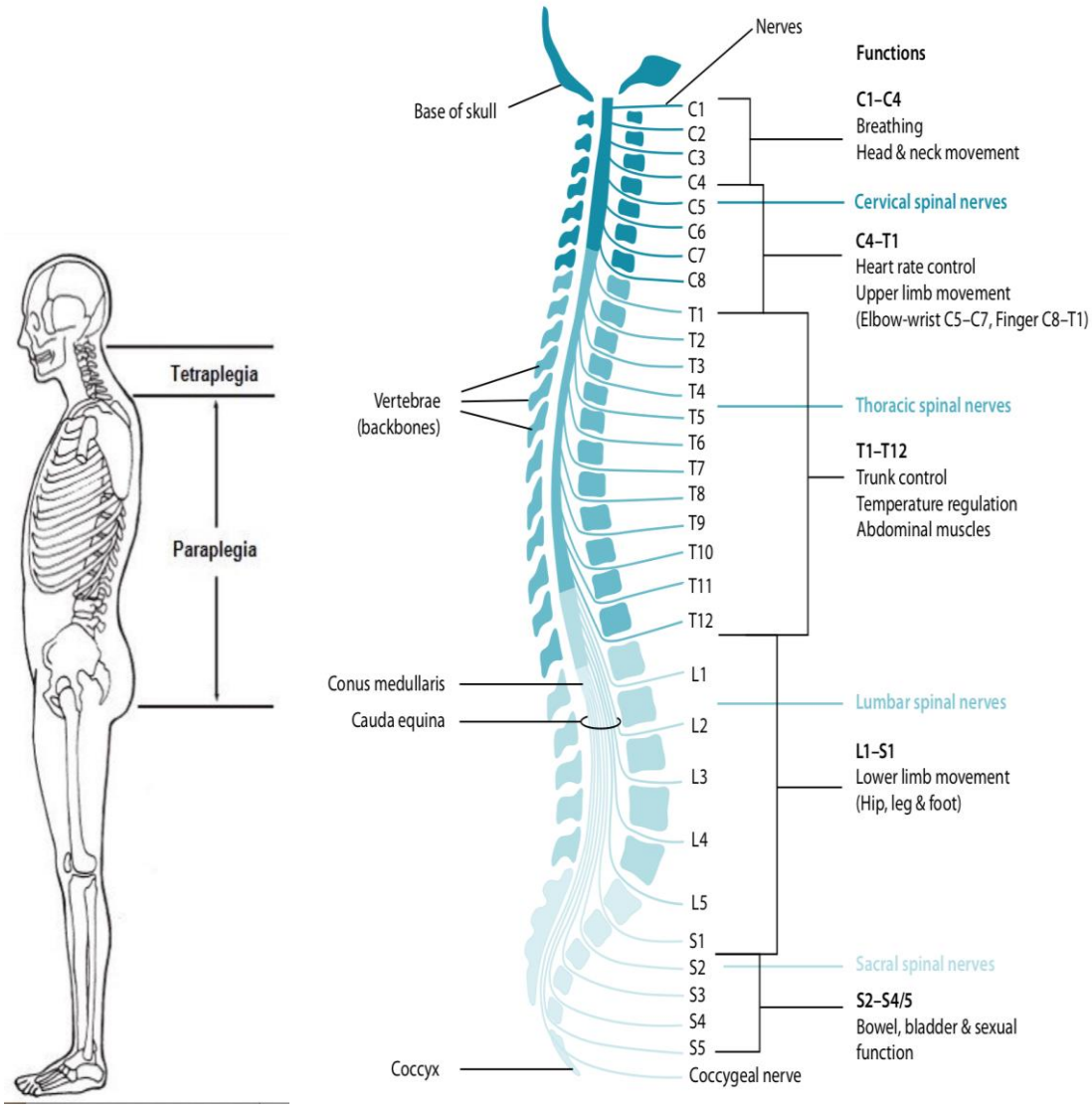

Figure 2 Levels of Spinal Cord Injury. The diagram on the left shows the resulting injury (either tetraplegia or paraplegia) from different levels of spinal cord damage. The diagram on the right shows the organisation of the spinal cord and the functions associated with it. Adapted from "*What is Spinal Cord Injury?" by* Motivation. Freedom Through Mobility, 2018, retrieved from https://www.motivation.org.uk/what-is-spinal-cordinjurysci?gclid=EAIaIQobChMIs7LKu5rA3gIVSbTtCh27ZAxeEAAYAiAAEgKqqvD_BwE. Copyright 2018 by Motivation Freedom Through Mobility; and from "*International Perspectives on Spinal cord Injury" by* World Health Organisation & International Spinal Cord Society, 2013, Geneva: World Health Organisation, p. 5. Copyright 2013 by the World Health Organisation.

Additionally, the damage to nerves prevents the reuptake of the excitatory neurotransmitter glutamic acid, allowing it to continue exciting nerves in the area. This opens calcium ion channels enabling positively charged calcium ions to flood into the cell, which can result in neuronal cell death. The speed of emergency treatment can determine the extent of the damage this causes (Belousov, 2012), but a spinal cord injury cannot be mended. The injury itself may be complete or incomplete. Complete injuries affect both sides of the body and result in a lack of muscle function and sensation from the level of the injury and below. According to the International Standards for Neurological Classification of Spinal Cord Injury (Kirshblum et al., 2011), to be classified as a complete injury there is no sensory or motor function at the S4 - S5 level. With an incomplete injury, which is much more common, some muscle function and sensation will be retained below the injury level including at the S4 - S5 level (Kirshblum et al., 2011). Despite these aspects of commonality the complexity of spinal cord injuries makes each one unique (World Health Organisation & International Spinal Cord Society, 2013).

The causes of spinal cord injuries are classified as being either traumatic or non-traumatic. The leading causes of traumatic spinal cord injuries (TSCI) are road traffic accidents and falls respectively, but they can also be caused by sporting and work-based injuries and by violence (World Health Organisation & International Spinal Cord Society, 2013). However, there are age related differences. Road traffic accidents are the leading cause of TSCI in younger people but for those aged over 60, falls become the leading cause (World Health Organisation and International Spinal Cord Society, 2013). In the United Kingdom it is estimated that the annual incidence of traumatic spinal cord injuries is 15 per one million and that half of these are at the cervical level, with the majority being incomplete (National Spinal Cord Injury Strategy Board, 2012). There is less information regarding the causes of non-traumatic spinal cord injuries (World Health Organisation and International Spinal Cord Society, 2013) but they can be caused by diseases such as tuberculosis, musculoskeletal diseases such as osteoarthritis, tumours, nutritional deficiencies such as vitamin B12, congenital problems or by complications during surgery or other medical care. Globally the leading causes seem to be

tumours and degenerative spinal conditions, with vascular and autoimmune conditions being the next most common (World Health Organisation and International Spinal Cord Society, 2013). For both traumatic and non-traumatic spinal cord injuries the incidence is higher in men than in women. However, unlike traumatic spinal cord injury, with non-traumatic SCI the incidence increases with age (World Health Organisation and International Spinal Cord Society, 2013). Whilst there is some consistency in the reporting of the most common causes of spinal cord injury across different regions of the world, the percentages vary hugely from region to region (World Health Organisation and International Spinal Cord Society, 2013) making the reporting of precise figures here meaningless. Additionally, there is no data on causes of spinal cord injury in the United Kingdom (UK) as a whole.

With a spinal cord injury, the level of injury determines the degree of disability, with higher level injuries resulting in more extensive symptoms. This can be seen in Figure 2. Cervical injuries refer to lesions between C1 and T1. Injuries between C5 and T1 result in varying degrees of paralysis in the arms, body and legs and is known as tetraplegia. If the injury is higher than C4 vital autonomic functioning may be impaired and, for example, a ventilator may be required for breathing. Thoracic injuries between T2 and T8 cause loss of function to the legs and can also result in poor trunk control, whereas trunk control is maintained in lower level injuries between T9 and T12. Lumbar injuries (L1 - L5) typically affect sensory and motor function in the legs and hips and damage to the sacral region, conus medullaris and cauda equina, whilst rarely causing complete paralysis, can result in weakness in the hips and legs and problems with bladder, bowel and sexual functioning. The International Standards for Neurological Classification of Spinal Cord Injury (ISNCSCI), produced by the American Spinal injuries Association (ASIA; 2011) identifies the type of disability associated with the level of injury. It is known as the ASIA Impairment Scale and classifies spinal cord injuries into the following 5 categories:

A: Complete. No sensory or motor function is preserved in the sacral segments S4-S5.
B: Sensory incomplete. Sensory but not motor function is preserved below the neurological level and includes the sacral segments S4-S5 (light touch, pin prick at S4-S5 or deep anal pressure), AND no motor function is preserved more than three levels below the motor level on either side of the body.
C: Motor incomplete. Motor function is preserved below the neurological level and more than half of key muscle functions below the single neurological level of injury (NLI) have a muscle grade less than 3.
D: Motor incomplete. Motor function is preserved below the neurological level and at least half of key muscle functions below the NLI have a muscle grade of 3 or greater.
E: Normal. If sensation and motor function as tested with the ISNCSCI are graded as normal in all segments, and the patient had prior deficits, then the AIS grade is E. Someone without an initial SCI does not receive an AIS grade.

American Spinal Injuries Association (2011)

The neurological level of injury (NLI) refers to the lowest level with muscle function and intact sensation, and the motor level refers to the lowest muscle level that has a muscle grade of 3 or above. A muscle grade of 3 is defined as one that has “active movement and a full range of motion against gravity” (ISNCSCI, American Spinal injuries Association, 2011).

3.1 Physical Symptoms of Spinal Cord Injury

Although spinal cord injuries are relatively rare, the consequences are life altering and go beyond paralysis. A range of other physical and psychosocial symptoms are commonly experienced. Where physical symptoms are concerned, most people have difficulties with autonomic functioning to some degree and this might commonly include problems with bladder, bowel and sexual functions, and difficulty regulating temperature, heart rate and blood pressure (Alexander et al., 2009). A sudden and dangerous increase in blood pressure (autonomic dysreflexia) might occur but orthostatic hypotension can

also be experienced manifesting in a sudden drop in blood pressure when sitting up (Krassioukov, Eng, Warburton, and Teasell, 2009). Urinary tract infections and pressure sores can be a particular problem carrying with them a higher mortality risk, and frequently requiring hospitalisation (Charlifue, Weitzenkamp, and Whiteneck, 1999; Cardenas, Hoffman, Kirschblum, & McKinley, 2004; Cardenas, Hoffman, Kelly, & Mayo, 2004). Urinary tract infections are the highest cause of septicemia, which itself is the second highest cause of premature death in this population (Soden et al., 2000). Broncho-pulmonary / respiratory functioning problems, where there is difficulty in breathing and clearing secretions through coughing, are also common and can lead to an increased risk of pneumonia (Winslow, & Rozovsky, 2003; Zimmer, Nantwi, & Goshgarian, 2007). This can be particularly dangerous as pneumonia and influenza have been found to be the leading cause of premature death for people with spinal cord injury (Soden et al., 2000). People with tetraplegia are at particular risk of these type of respiratory difficulties because the muscles associated with breathing may be paralysed.

In addition to these autonomic related problems, many people with SCI contend with spasticity involving involuntary movements and the development of contractures in joints, further reducing movement ability (Bryce, 2010). However, the most disabling secondary condition in spinal cord injury is pain (Bloemen-Vrencken, Post, Hendricks, De Reus & De Witte, 2005). A high number of people experience neuropathic and musculoskeletal pain (Dijkers, Bryce, & Zanka, 2009). A report into pain in Europe (Fricker, 2003) identified a prevalence of chronic pain in the general population of 19% in Europe as a whole and 13% in the United Kingdom. This figure increases dramatically in the spinal cord injured population where it has been estimated that over 62% experience chronic pain (Ullrich, Jensen, Loeser and Cardenas, 2007). Pain and spinal cord injury will be discussed in more detail in Section 4.3.

3.2 Psychosocial Symptoms of Spinal Cord Injury

Psychosocially, people with SCI experience a whole range of additional problems. Difficulties with activities of daily living might include problems with self-care, such as dressing, bathing and toiletting, with domestic activities such as cleaning and cooking, with maintaining employment or education, with engaging in leisure activities and with maintaining social relationships (World Health Organisation, 2001). This, together with the need to psychologically adapt to the spinal cord injury and the secondary physical problems associated with it, can lead to an increased risk of mental health problems. For example, it has been estimated that between 20% - 30% of people with SCI show clinical signs of depression (Post and van Leeuwen, 2012), with 36% being prescribed psychotropic medications, mostly antidepressants (Craig et al., 2015). Comorbidity is also high with many people experiencing high anxiety levels in addition to other psychological disorders, such as post traumatic stress disorder or depression (Craig et al., 2015).

These psychological problems can continue beyond the initial stages of rehabilitation. Rates of anxiety problems have been found to be almost 30% two years post-injury in longitudinal studies (Craig, Hancock and Dickson, 1994; Kennedy and Rogers, 2000). This is of concern because, whilst other causes of premature death have decreased, between 1980 and 2000 the rate of suicide increased by three times, with individuals with tetraplegia being at particular risk (Soden et al., 2000). A recent study found that death by suicide equated to 4.2% of all deaths for people with traumatic spinal cord injury, with people being particularly vulnerable within the first ten years following injury (Savic et al., 2018). This represents a much higher rate of suicide than in the general population placing this group at greater risk (Giannini et al., 2009). Suicidal ideation has been linked to the occurrence of major depression and once the depression was successfully treated, the thoughts of suicide diminished (Kishi, Robinson and Kosier, 2001), highlighting the importance of appropriate screening and diagnosis. Mental health and spinal cord injury will be discussed further in Section 6.4.4.

Although mortality rates depend on the proficiency of clinical and rehabilitation services, these secondary health and psychosocial conditions mean that people with SCI have a much greater mortality risk and are estimated to be two to five times more likely to die than the general population (Chamberlain, Meier, Mader, Groote and Brinkof, 2015). Effective rehabilitation is, therefore, crucially important in assisting in adaptation to the injury.

3.3 The Role of Appraisal in Adaptation to Spinal Cord Injury

A spinal cord injury results in many physical, psychological and social challenges, leading to a significant disruption in people's lives (Eaton, Jones and Duff, 2018). Successful adjustment is extremely important, and involves psychological and social processes (Eaton et al., 2018). Previously, it had been thought that adjustment was dependent on the length of time since injury (Guttmann, 1976). However, more recent research has proposed that cognitive appraisal of injury might be a more accurate predictor of adjustment (Dean and Kennedy, 2009). The Stress Appraisal and Coping Model (Lazarus and Folkman, 1984), which highlights the role of psychological and cognitive processes in adjustment to stressful situations, suggests that individuals make both primary and secondary appraisals. Initially, a primary appraisal about the event itself is undertaken considering whether the situation is threatening or not. Next, a secondary appraisal of the individuals own capacity to cope occurs, and this involves a consideration of whether available coping resources are sufficient for the situation.

It is thought that there are three dimensions of appraisal: threat, where the potential for harm is appraised; loss, where the likelihood of loss of health, friendships or self-esteem is appraised; and challenge, where the possibility of mastery or growth is appraised (Ferguson, Matthews and Cox, 1999). Threat and loss might represent primary appraisals of the situation and challenge might be associated with the secondary appraisal of ability to cope. Where appraisal of spinal cord injury is concerned therefore, the way in which the situation or injury is perceived can have a greater bearing on outcomes than

the event itself (Catalano, Chan, Wilson, Chiu and Muller, 2011). These appraisals can be influenced by external factors such as the extent of available social support, and by internal factors, for example, problem solving skills and previous experience (Holroyd and Lazarus, 1993).

The Stress Appraisal and Coping Model (Lazarus and Folkman, 1984) has been applied to the way in which people adjust to spinal cord injury (Galvin and Godfrey, 2001), placing cognitive appraisal as a key factor in adaptation. Additionally, cognitive appraisal may not just occur in the acute stages of rehabilitation, but continue over time, with re-appraisals being made as additional information is received (Duff and Kennedy, 2003). This is important because the way an individual appraises the situation can influence the degree to which their coping strategies will prove effective, but the effectiveness of their coping can then go on to influence further appraisals of the situation (Dean and Kennedy, 2009). In this way, coping processes can be influenced by appraisals but can in turn also influence them.

Dean and Kennedy (2009) have identified two overarching ways in which people appraise their spinal cord injury: catastrophic negativity consisting of fearful despondency, overwhelming disbelief, and negative perceptions of disability; and determined resilience consisting of determined resolve, growth and resilience, and personal agency. It has been suggested that ‘catastrophic negativity’ reflects the primary appraisals of the Stress Appraisal and Coping Model (Lazarus and Folkman, 1984), with threat and loss being the pertinent initial appraisals. The secondary appraisals, where available coping resources are considered might reflect ‘determined resilience’ (Mignogna, Christie, Holmes and Ames, 2015).

These two categories of appraisal have been associated with quality of life, with negative appraisals being inversely related and aspects of resilience being positively related (van Leeuwen, Kraaijeveld, Lindeman, and Post, 2012). More specifically, the negative cognitive appraisals associated with low quality of life include overwhelming disbelief and fearful despondency, along with a negative view of their own growth and resilience (Kennedy, et al., 2010).

In contrast, there is a positive correlation between resilience and life satisfaction (Quale and Schanke, 2010). A negative appraisal of injury does not just affect quality of life but has also been associated with poorer functional outcomes (explaining 49.4% of variance) where activities of daily living are concerned following discharge (Kennedy et al., 2010). Additionally, appraisals are thought to influence the type of coping strategies that people adopt following injury and have been associated with emotional well-being (Kennedy, Lude, Elfström and Smithson, 2010), indicating the importance of appraisals in longer term rehabilitation.

The association between appraisals and quality of life, emotional well-being and functional outcomes is not surprising. The events that cause a spinal cord injury as well as the considerable resulting alterations in physical independence are likely to be traumatic. The individual will also endure a significant period of time in hospital with a focus on extensive rehabilitation, and often have to deal with loss in terms of employment role, community role or their role within the family (Martz, Livneh, Priebe, Wuermser and Ottomanelli, 2005). As such, individuals may appraise the stressors as being too significant and as exceeding their ability to cope. It is, therefore, also unsurprising that psychological disorders are experienced by many (Bonanno, Kennedy, Galatzer-Levy, Lude and Elfström, 2012).

Scores on the Appraisal of Disability Primary and Secondary Scale (ADAPSS; Dean and Kennedy, 2009), which measures catastrophic negativity and determined resilience, have been positively and negatively associated with symptoms of depression respectively (Mignogna et al., 2015). Appraisals more generally have been associated with anxiety and depression, explaining 12% and 34% of variance respectively, and predicting future adjustment to SCI (Kennedy, Evans and Sandhu, 2009). Both anxiety and depression have been negatively associated with psychological adjustment suggesting that cognitive appraisals could be an important factor to assess and target in rehabilitation (Dean and Kennedy, 2009). This has been supported more recently with appraisals made during rehabilitation accounting for greater variance in anxiety and depression than biological markers or the characteristics of the

injury (Eaton et al., 2018).

Intuitively it might be expected that a lower level of injury, and therefore greater functioning, would predict more positive appraisals of the injury, whereas research suggests that this protective factor does not exist (Mignogna et al., 2015). In fact the most catastrophic negativity was found in veterans with lower injury levels (Mignogna et al. 2015), although it is not clear why this should be. It is possible that the individual's perception is that they should be able to cope better, thus causing greater distress and negative appraisal when this is not the case. What it does suggest is that level of injury might not be a reliable predictor of better adaptation, and that regardless of level of injury screening of cognitive appraisals should be an important part of rehabilitation services.

Longitudinally, negative appraisals and maladaptive coping strategies adopted during the acute stages of rehabilitation have been negatively associated with psychological distress two years post injury (Kennedy, Lude, Elfström and Smithson, 2010) and been found to predict psychological distress and appraisal 21 years post injury (Kennedy, Kilvert and Hasson, 2016). Additionally, lower functional independence has been associated with negative appraisals (Kennedy et al., 2010). The importance of resilience has also been established longitudinally. Six months following discharge people with SCI and high resilience are up to five times less likely to have a psychological disorder such as anxiety and depression than those with lower resilience and less likely to have comorbid psychopathology (Craig et al., 2015). Resilience has been associated with more positive emotions and lower catastrophizing (Ong, Zautra and Reid, 2010). Positive emotions have been found to predict better adaptation to stressful situations and a faster recovery from such events (Ong, Bergeman, Bisconti, and Wallace, 2006).This indicates that appraisals made soon after the injury might have long-term consequences for both physical and psychological adaptation. Measures of appraisal are therefore important prior to discharge in order to identify possible future risks of this nature. Additionally, an examination of how appraisals change over time and at transition to the community would inform the type of on-going support that might be required.

Lazarus and Folkman (1984) suggested that when a person appraises a situation as threatening and concludes that they do not have the ability to cope with it, they are more likely to engage in unhelpful coping strategies such as avoidant or passive coping. This has been supported more recently in spinal cord injury, with a significant relationship being found between coping, appraisals and functional outcomes, where negative appraisals were strongly associated with social reliance. In turn, social reliance was negatively correlated with functional independence (Kennedy, Lude, Elfström and Smithson, 2011). Social reliance has been defined as considering oneself dependent on other people for support, and being helpless without that support (Kennedy, Lude, Elfström and Smithson, 2010). This impacts negatively on individuals' engagement with the rehabilitation process, and additionally, poorer coping and negative appraisal have been associated with poorer psychological outcomes, as previously stated (Kennedy et al., 2010). This could also impact negatively on rehabilitation efforts as people may have reduced motivation to engage. This suggests that focused support may be necessary for individuals who are identified as being more likely to engage in passive or avoidant coping.

It has been proposed that interventions targeting coping strategies and designed to improve resilience should therefore be utilized (Catalano, Chan, Wilson, Chiu and Muller, 2011). For example, coping effectiveness training has been successful in reducing depression and anxiety symptoms in people with spinal cord injury (Kennedy, Duff, Evans and Beedie, 2003). This is important because being able to participate in meaningful activities and being able to continue to strive towards achieving meaningful goals have been associated with positive adjustment to spinal cord injury (Edhe, 2010).

When considering the facilitators of adjustment, resilience has been identified as one of the key factors (Duggan, Wilson, DiPonio, Trumpower and Meade, 2016). Resilience has been defined as the ability to adapt to adverse situations, and is likely to involve specific skills alongside stable temperament and personality variables such as extraversion and dispositional optimism

(Ramírez-Maestre and Esteve, 2013). This suggests that resilience may itself be a stable multidimensional trait (Ramírez-Maestre and Esteve, 2013). As well as being an important factor where appraisal of injury is concerned, resilience is also important where pain is concerned because it has been associated with the utilization of better coping strategies and a more positive attitude towards pain (Sturgeon and Zautra, 2010). Additionally, resilience and pain acceptance have been closely associated (Biglan, Hayes and Pistorello, 2008; Ramírez-Maestre, Esteve and López, 2012), with resilience predicting greater pain acceptance, and greater pain acceptance predicting better coping and adjustment to chronic pain (Ramírez-Maestre et al., 2012). This has been supported more recently with positive correlations being found between acceptance, adjustment to pain and resilience (Ramírez-Maestre, Esteve, and López-Martínez, 2014). It is likely therefore, that resilience is a significant resource in an individual's ability to adjust to injury and to manage pain, and is therefore an important variable to include in the study of pain conditions in people with SCI. Identifying what helps people to cope effectively is as crucial as understanding what impacts negatively on the injury and pain experience.

In contrast to Ramírez-Maestre and Esteve (2013), The American Psychological Association (APA; 2019) defines resilience as

> the process of adapting well in the face of adversity, trauma, tragedy, threats or significant sources of stress…It means "bouncing back" from difficult experiences… Resilience is not a trait that people either have or do not have. It involves behaviors, thoughts and actions that can be learned and developed in anyone. (American Psychological Association, 2019, The Road to Resilience, What is Resilience section, para. 1)

This definition clearly states that anyone can develop resilience; it is not something that individuals are born with, which supports earlier studies suggesting that it is possible to acquire the characteristics of resilience, and that it is not a stable personality trait (Kumpfer, 1999; Newman, 2005). It is possible that certain personality characteristics, such as openness to

experience or extraversion for example, make people more likely to have a propensity for resilience in the face of adversity, but that resilience strategies can also be developed in those who are more vulnerable. As a concept closely associated with adjustment, this is an important consideration for rehabilitation. Duggan et al. (2016) in their qualitative study identified certain facilitators and barriers to resilience in spinal cord injury. Facilitators included adaptability, previous experience of adversity, personal growth and persistence. Barriers were identified as ageing and number of years living with a spinal cord injury, the number of concurrent challenges being faced, the belief that no one really bounces back following a trauma, and chronic pain (Duggan et al., 2016). Additionally, participants in the study highlighted that they frequently used cognitive restructuring as a way of increasing resilience. The key component of cognitive restructuring is the appraisal of a negative situation in a way that is more helpful to the individual, once again highlighting the important role appraisal has in the process of adjustment.

The factors that mediated resilience align with those identified in the Posttraumatic Growth Inventory (Tedeschi and Calhoun, 1996): relating to others; new possibilities; personal strength; spiritual change; appreciation of life. This suggests that posttraumatic growth and resilience may represent a single construct, or at least that they each have features that are necessary for the achievement of the other. Posttraumatic growth concerns the degree to which individuals perceive that they have benefitted in some way from their traumatic experience. This might include changes in the way they view their lives, their personal relationships and the way they view themselves. These changes are perceived to have resulted from the way the individual coped with the trauma (Tedeschi and Calhoun, 1996). This has similarities to the definition of resilience, stated above, and provided by the APA (2019), alluding to the notion that people can bounce back from adversity, supporting the idea that resilience and post traumatic growth may be similar constructs, rather than being exactly the same thing.

Reich and Zautra (2010) add weight to the association between post traumatic growth and resilience, suggesting that resilience can lead to three different

types of outcomes. Recovery is associated with the degree to which an individual returns to premorbid levels, both physiologically and psychologically following a stressful event. Sustainability refers to how well the individual maintains their social networks and continues to pursue goals and activities that support positive self-esteem and positive affect. Growth relates to the learning and increased self-understanding that can occur as a result of coping during a stressful period. In achieving these outcomes it is possible that resilience may reflect both a stable trait, and one that can be developed or learnt as suggested previously: resilience resources that include stable personality traits such as optimism and extraversion, but also stable social environments with ongoing support from family and friends, and a sense of purpose and meaning in life; and resilience mechanisms that are utilized in response to a stressful situation and include helpful thinking, behaviours and emotional responses that assist in maintaining well-being and enabling growth, and that can be developed (Sturgeon and Zautra, 2010). Figure 3 is a conceptual framework, which demonstrates how resilience resources can lead to resilience mechanisms being adopted (Sturgeon and Zautra, 2010). These mechanisms then moderate the relationship between pain and the resilient outcomes by improving the coping strategies utilized (Sturgeon and Zautra, 2010).

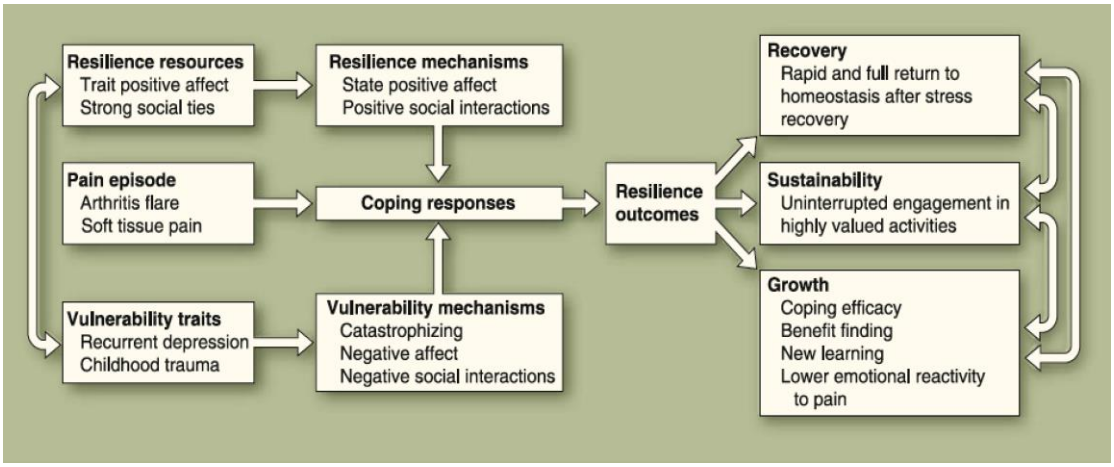

Figure 3: Conceptual diagram demonstrating the possible pathway, from resilience resources through resilience mechanisms and coping responses, to resilience outcomes following pain episodes. The items listed below the pathways are examples. From “Resilience: A new paradigm for adaptation to chronic pain,” by J. A. Sturgeon and A. J. Zautra, 2010, *Current Pain and Headache Reports, 14*, p. 107. Copyright 2010 by Springer Science+Business Media, LLC.

Resilience mechanisms are key in mitigating against the psychological distress identified as vulnerability traits in Figure 3, and improving outcomes of adaptation (Bonanno, 2004). Those demonstrating resilience cope better with the physical and psychological challenges of adjustment and rehabilitation (Bonanno, Kennedy, Galatzer-Levy, Lude, and Elfström, 2012). What is more, these gains continue beyond rehabilitation through to transition to the community. Some people experience a delayed psychological response to trauma, including spinal cord injury, where depression and anxiety symptoms are lower initially but increase over time (Bonanno, 2004). However, these people still exhibit greater symptoms of psychological distress early in rehabilitation than those with more resilience (Bonanno et al., 2012), suggesting that resilience may protect people over time. It is noticeable that people with higher resilience tend to be more likely to appraise their spinal cord injury as a challenge rather than a threat, and have greater acceptance of their SCI, demonstrating more of a fighting spirit than those exhibiting higher levels of anxiety and depression (Bonanno et al., 2012).

Where appraisal is concerned, it has been proposed that a balance of protective and risk factors will influence the degree of resilience exhibited. If it is appraised that there are many risk factors, then a higher quantity of perceived protective factors need to be present to compensate (Catalano et al., 2011). One such protective factor has been identified as social support (discussed in Section 7), which has been found to have a direct effect on resilience. Resilience in turn mediates the effect of stress on depressive symptoms (Catalano et al, 2011). This indicates the way in which social support impacts on psychological outcomes of SCI, and highlights the important mediating role that appraisal in the form of resilience plays in this.

3.4 Conclusion

As has been described, the effects of spinal cord injury can be devastating for individuals and their families, with serious, and sometimes life-threatening, physical and psychological sequelae. These secondary conditions can have

an important influence on how well an individual adjusts to their injury. One factor that can impact positively or negatively on adjustment is the way the injury is appraised; either with catastrophic negativity or with resilience. The effects of appraisal are far reaching, impacting on mental health, perceived quality of life, and functional independence. Research into the influence that appraisal of injury has on psychological and adjustment outcomes in pain conditions and in spinal cord injury demonstrates the importance of including measures of both catastrophic negativity and resilience in a study such as this. Appraisal has been shown to be important in pain conditions and separately in spinal cord injury, but how it might form a bridge between the two has yet to be established. Therefore, the way in which appraisal of injury combines with other variables that impact on adjustment and pain related outcomes in SCI needs to be established in order for effective treatment options to be available.

4 Chapter 2 - Understanding Pain

Pain is a problem affecting many people from all ethnic and socioeconomic backgrounds. It has recently been estimated that nearly 28 million adults, approximately 43%, experience ongoing pain in the United Kingdom (Fayaz, Croft, Langford, Donaldson and Jones, 2016). The International Association for the Study of Pain (IASP, 1994, p. 209) has defined pain as “an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage”. This definition acknowledges that the perception of pain is a two-fold process (Vitor et al., 2008). The first stage is nociception (sensory) where information about the painful stimuli is transmitted to the central nervous system. The second stage involves the more complex processing of this information which results in the conscious pain experience (emotional).

Pain can be characterised as being either acute or chronic. Acute pain usually stems directly from tissue damage, is short-lived in that it reduces in intensity over time and has a damage limitation role (IASP, 1994); pain motivates the sufferer to adopt pain avoidance strategies to reduce the risk of further damage, and to alert the sufferer to the possible presence of disease (Lumley et al., 2011). The intensity of this type of pain is often related to the extent of the injury or disease; the greater the severity, the greater the pain. Chronic pain is defined as pain that has persisted for three months or more and is more complicated than acute pain (IASP, 1994), for example, in contrast to acute pain, chronic pain may not have a known pathological cause and tends to be resistant to modern pain relief medication (Lumley et al., 2011). Pain has been categorised in three ways: physiological or nociceptive pain, inflammatory pain (similar to nociceptive pain but the tissue damage leads to white blood cells releasing chemicals that are normally protective, but which can result in fluid seeping into the tissue causing swelling and pain) and pathological or neuropathic pain (Woolf and Salter, 2000). This thesis focuses on nociceptive and neuropathic pain.

4.1 Nociceptive Pain

Physiological pain is also referred to as nociceptive pain because it occurs as a result of stimulation of the pain receptors called nociceptors that are located in muscles, joints and skin. These are stimulated when some sort of trauma or injury is received. When this occurs, pain messages are transmitted to the dorsal horn in the spinal cord via two types of afferent nerve (Vitor et al., 2008). A delta (Aδ) myelinated nerve fibres send location specific information about sharp pain, providing a fast pathway, which enables a quick response such as a withdrawal reflex to avoid further tissue damage. C poly-modal (responding to stimulation from different modalities) nerves are unmyelinated and provide a slow pain pathway for the burning or dull pain that often follows a sharp pain. These fibres respond to mechanical, thermal and chemical stimulation of the skin. The messages via the C fibres provide less detailed location information making it hard to identify exactly where the pain is coming from. Additionally, there are larger afferent nerves called A beta (Aβ), which are myelinated, and respond to non-noxious or tactile stimuli. Information is carried by these three nerve fibres to the cells of the dorsal horn in the spinal cord where pain processing begins.

Once the neurons in the dorsal horn are activated, the pain signal travels to the thalamus in the forebrain via the anterior lateral system. This consists of four pathways: the anterior and lateral spinothalamic tracts, the spinoreticular tract and the spinomesencephalic tract (Millan, 1999), as depicted in Figure 4. The spinothalamic tract receives information from the Aδ and C fibres. The anterior spinothalamic tract transmits this information via the ventral posterior lateral and inferior thalamic nuclei to the somatosensory cortex, providing information about the location of the painful stimulus (‘where’ information). The lateral spinothalamic tract projects to various brain structures including the periaqueductal grey (PAG), the somatosensory cortex, the thalamus, the insula, the anterior cingulate cortex as well as the amygdala and hypothalamus. It provides information about the emotional and affective qualities of the pain (‘what’ information). The spinoreticular tract sends information to the dorsal thalamus via the reticular formation of the brainstem

(Sengul and Watson, 2012). This enables appropriate arousal in response to the pain and also has a role in controlling descending pain modulation (Millan, 1999). The spinomesencephalic tract projects to the PAG, which has connections with the limbic system via the hypothalamus. Together with the spinoreticular tract, it has a role in the control of pain processing (Vitor et al., 2008).

All pain information transmitted by the anterior lateral system passes through the thalamus. The thalamus acts as a relay station for all the sense modalities (apart from the olfactory system), and where pain is concerned it has the function of integrating the different pain signals and sending them on to various areas of the cortex. This results in the perception of pain (Fürst, 1999). Two parts of the thalamus are particularly important. The ventral thalamus sends detailed and accurate pain information to the primary sensory cortex in the parietal lobe, which is then transmitted to the secondary and association cortices for further processing. It is known as the “slow and accurate” system (Møller, 2014, p. 92). The Dorso-medial thalamus by-passes the primary sensory cortex, sending information straight to the secondary and association cortices, and also to parts of the limbic system such as the amygdala, inferior cingulate cortex and the hippocampus. This information is less detailed and accurate and as such is called the ‘fast and dirty’ system (Møller, 2014, p. 92). It is involved in the emotional response to pain (Sacco and Sacchetti, 2010).

Along with these physiological ascending pain pathways, pain perception can be influenced by a descending central modulating system as shown in Figure 4. This system is able to facilitate or inhibit the pain messages, and which it does results from the balance between inhibitory and excitatory activity.

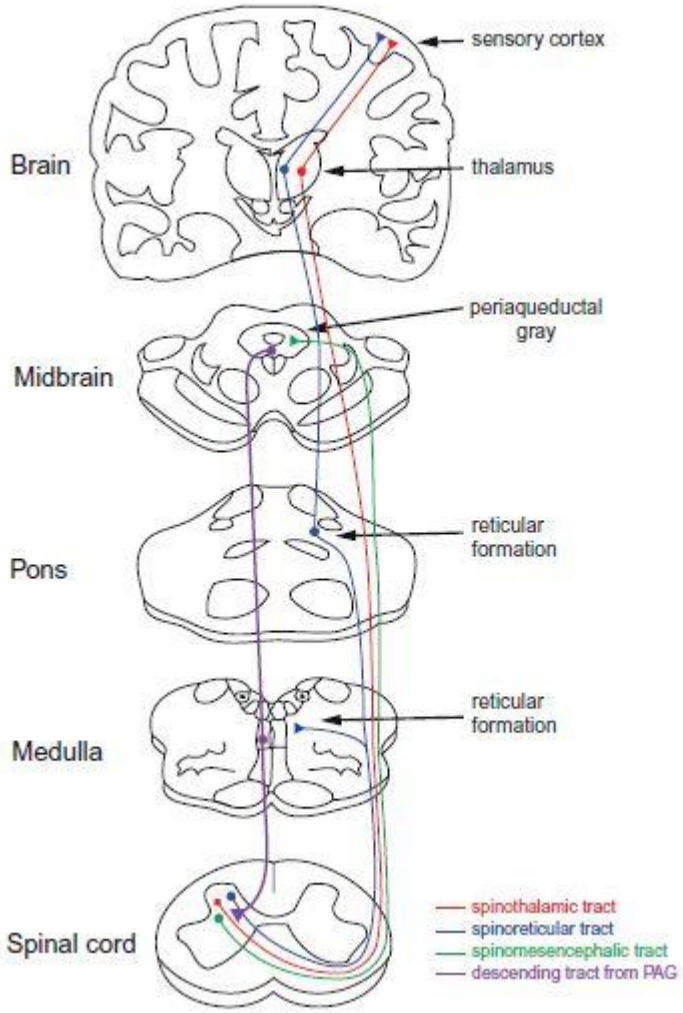

Figure 4. Schematic representation of the anterior lateral system. Depicts the spinothalamic tract (in red), the spinoreticular tract (in blue), the spinomesencephalic tract (in green) and the descending tract from the periaqueductal grey (in purple). From “Pain Genetics”, by W. Renthal, 2015, in R. N. Rosenberg and J.M Pascual (Eds.), *Rosenberg’s Molecular and Genetic Basis of Neurological and Psychiatric Disease, Fifth Edition.* pp. 1089-1100. Waltham Massachusetts: Academic Press.

A key structure involved in pain modulation is the ventral PAG. When stimulated, it sends impulses to the neurons of the rostral ventromedial medulla (RVM) and the dorsolateral pontine tegmentum (DLPT). The RVM releases the neurotransmitters serotonin and encephalin, which inhibit activation of the neurons in the dorsal horn, reducing the response to pain (Basbaum and Jessell, 2000). In contrast, the noradrenergic DLPT has an excitatory effect. However, both the RVM and the DLPT can facilitate or inhibit

pain impulses. Additionally, the locus coeruleus activates noradrenergic neurons in the dorsal horn inhibiting pain transmission (Belcher, Ryall, and Schaffner,1978). In this way, the experience of nociceptive pain involves both bottom-up processes, where pain signals are sent through the spinal cord to the brain, and top-down processes where the conscious experience or perception of pain is modulated. This modulation can be influenced by the situation the individual is in and by various psychological variables. This was first reported by Beecher (1946) in an analysis of pain experienced by wounded soldiers during the second world war. He found that despite having very severe injuries many of them did not require pain relief medication. Beecher concluded that knowing they were going to be taken away from the battlefield to a place of safety moderated the pain they felt, suggesting that their appraisal and other cognitions were influential in how severe they rated their pain to be. Such psychological variables are discussed in Chapter 4.

4.2 Neuropathic Pain

When nociceptors are not involved in the perception of pain, this is referred to as pathological and a common form of pathological pain is neuropathic pain. The International Association for the Study of Pain (IASP) defines neuropathic pain as “pain that arises as a direct consequence of a lesion or diseases affecting the somatosensory system” (Jensen et al., 2011, p. 2204). Although neuropathic pain often follows an injury of some sort, it is not caused by stimulation of pain receptors, but by abnormal functioning of the central and / or peripheral nervous systems (Møller, 2014). It is often persistent, and as such is thought of as a chronic pain condition (Møller, 2014). It has been estimated that the prevalence of neuropathic pain in the general population is between 6.9% and 10% (van Hecke, Austin, Khan, Smith and Torrance, 2014), but it is difficult to be precise because the presence of neuropathy in an individual reporting pain is not always apparent, making this type of pain difficult to diagnose (van Hecke et al., 2014). Additionally, because neuropathic pain does not rely on the transmission of pain signals in the same way nociceptive pain does, it is resistant to pain medication making it difficult to treat (Tölle, 2010). Individuals may experience this type of pain with varying

intensity, and frequently it can present with hyperpathia (an exaggerated pain response to light or moderate pain stimulation), allodynia (pain from a gentle stroke or touch) and hyperalgesia (a lower pain threshold) (Sandkühler, 2009). Sufferers of neuropathic pain may also experience the 'wind-up' phenomenon whereby repeated stimulation of neurons in the dorsal horn leads to an increase in perceived pain intensity (Mendell and Wall, 1965). This is a form of temporal integration; each successive pain signal results in a stronger pain sensation and as such is the opposite of adaptation where perception of a sensation reduces with on-going and repeated stimulation (Møller, 2014).

Far less is known about neuropathic pain than nociceptive pain although theories such as the neuromatrix theory of pain (Melzack, 1993) attempts to explain what could be causing it (see 'Biological Theories of Pain' below). However, the fact that neuropathic pain and other chronic pain conditions may not be caused by an internal or external noxious stimulus suggests that other causes or factors must be involved. This conflicts with some of the very early theories of pain. Developing from Descartes (1664), Specificity Theory (von Frey, 1894) simply suggested that pain signals are sent along specific Aδ and C poly-modal fibres, via the spinothalamic tract, to the brain. In contrast, Pattern Theory (Goldscheider, 1894) suggested that the stimulation of nociceptive receptors triggers a pattern of neural firing, which is summated in the dorsal horn of the spinal cord. If the neural firing reaches a certain threshold, the pain information is sent to the brain. Both of these theories are considered to be 'direct line of transmission theories' (Marks, Murray, Evans and Estacio, 2011) where the level of pain experienced is believed to be directly linked to the severity of physical damage. They can only, therefore, explain nociceptive pain.

Research into pain over the past five decades has discovered that both of these theories are too simplistic and that pain involves many biological, psychological and social factors that interact in a complex way, and which are not taken into account in the direct line of transmission theories. In introducing the biopsychosocial model of health, Engel (1977) questioned whether the biomedical model of illness was sufficient as a model for medicine. He

highlighted the fact that it took no account of psychological or social factors yet it is well known that in illnesses such as diabetes and schizophrenia environmental and lifestyle factors have a significant influence on the onset of the disease and its progression (Kolb and Martin, 2017; Heald et al., 2017). Becoming ill and returning to good health, therefore, require more than simply attending to the somatic aspects of the illness (Engel, 1977). The social context of the patient, their behaviours and their affective experience of the illness also need to be considered and this is the same where pain in spinal cord injury is concerned.

4.3 Pain and Spinal Cord Injury

Individuals with spinal cord injury commonly experience both nociceptive and neuropathic pain, with recent prevalence estimates varying between 61% and 76% (van Gorp, Kessels, Joosten, van Kleef, and Patijn, 2015; Finnerup et al., 2016) indicating how common this secondary condition is. Severe pain will be experienced by approximately one-third of these people (Siddall, McClelland, Rutkowski, and Cousins, 2003). Earlier prevalence estimates of chronic pain have varied by as much as between 25% and 96% (Dijkers, Bryce and Zanca, 2009). This variation in prevalence estimates might be due to the heterogeneity between studies. For example, van Gorp et al., (2015) found a negative correlation between reported pain prevalence and how strictly pain was defined, with the stricter definitions being associated with lower prevalence of pain being reported. Additionally, higher pain prevalence was reported in studies whose primary focus was pain and in studies that took place longer after the original injury was obtained. Variation can also occur depending on whether neuropathic or nociceptive pain is the focus, although recently both types of pain were found to be present one-year post injury in 59% of patients (Finnerup et al., 2016). Prevalence rates of pain cannot therefore be precisely stated. Regardless of this, pain has been identified as the most cited problem where general functioning is concerned by people with spinal cord injury (Rubinelli, Glässel, and Brach, 2016).

Pain associated with spinal cord injury may be experienced immediately

following the injury or occur some time later (Jensen, Chodroff and Dworkin, 2007), with neuropathic pain sometimes developing years after the injury (Calmels, Mick, Perrouin-Verbe, and Ventura, 2009). Onset of pain is further complicated by the fact that at-level neuropathic pain seems to begin in the immediate days and weeks following injury, whereas below-level pain has an onset of months or years later (de Miguel, 2009; Siddall et al., 2003). Research has found that nociceptive pain is likely to reduce over time whilst neuropathic pain may worsen, or at best remain stable (Finnerup et al., 2014). This supports previous research where neuropathic pain was found to remain stable four years after discharge (Vassend, Quale, Røise, and Schanke, 2011). Frequently people report having multiple pain sites, increasing the difficulties they experience (Turner, Cardenas, Warms and McClelland, 2001). This is problematic because both pain related to SCI and its pharmacological treatment can be long-lasting, with only a small likelihood of achieving a pain-free state (Hagen and Rekand, 2015).

Historically there have been inconsistencies in the definitions of spinal cord injury pain used, adding to the complexity (van Gorp et al., 2015). Pain can be classified in terms of its affective and sensory dimensions. The affective dimensions relate to the emotional response to pain and to how unpleasant the pain is perceived to be. The sensory dimension of pain is concerned with the intensity and location of pain. It has been suggested that the affective dimensions of pain have a closer association with suffering and distress than the sensory dimensions (Gruener et al., 2018). The International Spinal Cord Injury Pain (ISCIP) Classification (Bryce et al., 2012) offers a method of classifying pain that can be used by clinicians and researchers and that should improve diagnosis and treatment and enable better communication between academic and health professionals in this area (Bryce et al., 2012). It categorises four types of spinal cord injury pain: nociceptive pain, neuropathic pain, other pain and unknown pain. Of interest to this study is the classification of nociceptive and neuropathic pain.

Nociceptive pain is defined as pain resulting from the activation of nociceptors and can be musculoskeletal (such as in muscles and joints), occurring in an

area where there is still sensation, or visceral, such as in the abdomen or pelvis (Bryce et al., 2012). Musculoskeletal pain may be a consequence of muscle damage or spasm, spinal fractures or arthritis, and is likely to worsen with movement and on palpation. Visceral pain may stem from problems such as constipation or urinary tract infections for example, and can be identified by a relationship with food intake, tenderness of visceral areas when palpated and /or the presence of nausea and sweating (Bryce et al., 2012). The most common type of nociceptive pain is musculoskeletal, which is likely to be responsive to anti-inflammatory and opioid medications (Bryce et al., 2012). This is often experienced in the upper extremity such as shoulders, elbows, wrists and hands and typically results from activities such as transferring from wheelchairs and wheelchair propulsion. (Cardenas and Felix, 2009). It has been estimated that approximately 58% of spinal cord injured people experience some upper extremity pain (Dalyan, Cardenas and Gerard, 1999), although shoulder pain prevalence has been reported in up to 78% of individuals (Silfverskiold and Waters, 1991). Back pain is another common type of musculoskeletal pain with an estimated prevalence of at least 60% (Turner, Cardenas, Warms and McClellan, 2001). The number of people reporting back pain does not vary significantly across different injury levels which implies it is a widespread problem possibly stemming from muscle strain and limited movement (Turner et al., 2001). Nociceptive pain is detrimental to well-being because it can interfere with essential functional activities such as transferring from wheelchairs and other activities of daily living (Dalyan, Cardenas and Gerard, 1999).

Of the two types of pain, however, neuropathic pain is thought to be the most debilitating, affecting between 49% and 53% of people with SCI (Finnerup et al, 2016; Burke, Fullon and Lennon, 2017). As stated previously, it is caused by a “lesion or disease of the somatosensory nervous system” (Jensen et al., 2011, p. 2204). Where spinal cord injury is concerned, research has determined that neural changes occur in the spinal cord following the injury. For example, nerve cells in the spinal cord close to the injury site exhibit abnormal activity such as greater responsiveness to stimulation, and prolonged firing (Christensen, Everhart, Pickelman, and Hulsebosch, 1996).

This can result in an over-amplification of pain messages or neurons sending pain messages on their own, without those messages coming from nociceptive signals (Siddall, McCabe and Murray,2014). Additionally, spinal cord injuries can damage the descending inhibitory mechanisms, described in Section 4.1, so that they are no longer able to lower the volume of these pain messages. This can mean that nociceptive pain signals are also stronger, so damaged inhibition impacts negatively on both neuropathic and nociceptive pain experiences (Siddall,et al., 2014).

Neuropathic pain is pain that presents either below the level of injury or at the level of injury, with most falling below the level of injury (Burke, Fullon and Lennon, 2017). A dermatome is the area of skin supplied by a single spinal nerve root. At-level neuropathic pain is defined by ISCIP as pain occurring within three dermatomes below the neurological level of injury (NLI) or in the dermatome of the NLI. If pain is present in these areas then pain at the dermatome one level above the NLI is also classified as being at-level. In contrast, below-level neuropathic pain occurs more than three dermatomes below the NLI. If it occurs in this area but also in the levels at and immediately below the NLI it is still classified as below-level. Characteristics of at-level and below-level neuropathic pain are the same and include allodynia or hyperalgesia and pain described as burning, pricking, sharp and electric shock-like (Bryce, et al., 2012). In contrast to nociceptive pain, neuropathic pain can be influenced by attention and mood, tends to be constant and unrelated to movement (Widerström-Noga, Cruz-Almeida, Felix and Adstock, 2009).

Neuropathic pain occurs more frequently in older individuals and those with tetraplegia rather than paraplegia (Burke, Fullon and Lennon, 2017). This is in contrast to previous studies that found that younger age was predictive of pain more generally (Finnerup et al, 2016). Neuropathic pain is often experienced as being severe, and because of this it can have a significant effect on quality of life and the ability to carry out daily activities (Gruener, Zeilig, Laufer, Blumen and Defrin, 2018). Additionally, the presence of neuropathic pain has been associated with higher levels of distress manifesting as pain

catastrophizing, depression and anxiety compared to people with similar SCI characteristics but without pain (Gruener et al., 2018; Otis, Marchand, and Courtois, 2012). This suggests that the psychological distress experienced by people with SCI and pain may be more closely related to the pain rather than resulting from the injury. This has been borne out in qualitative studies where it has been described as “exhausting, agonizing and cruel” (Gruener et al., 2018, p. 181) and as an uncontrollable attack by something malevolent (Hearn, Finlay and Fine, 2016), demonstrating the distress that can be caused by neuropathic pain. This is particularly important given that once it has developed, generally within the first year following injury, it does not then seem to improve (Finnerup et al., 2016). Of additional concern is that neuropathic pain has been found to respond poorly to pharmacological remedies (Teasell, et al., 2010), making it difficult to treat.

Individuals with SCI and chronic pain have reported experiencing high pain intensity on most days and significant difficulty in coping with that pain (Craig, Guest, Tran, Nicholson Perry and Middleton, 2017). This can lead to lower mood, higher anxiety, lower resilience and greater use of medications (Craig et al., 2013; Nicholson Perry, Nicholas, Middleton and Siddall, 2009; Widerström-Noga et al., 2016). In turn, difficulties in coping, lower resilience and poor communication about treatment options predict greater difficulty in dealing with pain (Widerström-Noga et al., 2016). In a recent meta-analysis, pain was associated with higher levels of stress and depression, poorer coping strategies, a lower belief in the ability to manage self-care activities and a lower likelihood of employment, and consequently financial independence (Tran, Dorstyn, and Burke, 2016). However, pain can have far reaching effects that go beyond psychological issues and adaptation to injury. Pain has also been associated with greater difficulties reintegrating into the community upon discharge from rehabilitation (Donnelly and Eng, 2005) and reduced social support and interaction (Erosa, Berry, Elliott, Underhill and Fine, 2014). This indicates that pain might alter the way individuals interact with others, but it could also alter the way others interact with the individual. These studies support previous research that suggests that the greatest predictor of social integration and psychological functioning was pain (Jensen, Moore, Bockow,

Ehde and Engel, 2011).

Pain has also been associated with poorer working memory and reduced executive functions, such as planning, organizing and decision making (Berryman et al., 2013; Berryman et al., 2014). These functions are important in carrying out the cognitive tasks necessary for successful rehabilitation and as such may interfere with goal planning and the utilization of appropriate coping strategies (Schmidt, 2016), adding to the difficulties in social integration. Of note is that after discharge from inpatient rehabilitation many of these problems associated with pain can continue to worsen (Craig et al., 2015). For example, it has been found that pain catastrophizing and pain intensity, whilst decreasing during rehabilitation, increase after transition to the community (Craig et al, 2017). This might in part be due to the social environment in the community, where there is a lack of professional support available, resulting in personal coping resources being challenged (Craig et al., 2017). However, individuals who are able to accept their pain and live a full life despite the pain seem to have a more positive outcome. Activity engagement, one of the factors of pain acceptance, predicts reduced depression and interference from pain, as well as a greater satisfaction with social engagement and a better quality of life (Kratz, Hirsh, Ehde, and Jensen, 2013). This suggests that the treatment of pain requires a focus on the psychosocial factors as well as the biological aspects associated with pain.

This need for a biopsychosocial approach to the treatment of pain has been recognised for some time, however the medical model still prevails (Widerström-Noga, Finnerup and Siddall, 2009). The most common treatments of both types of pain in spinal cord injury continue to be pharmacological (Heutink, Post, Wollaars, and Van Asbeck, 2011). Opioids and non-steroidal anti-inflammatory drugs (NSAID) are frequently used for musculoskeletal pain and can be effective in the acute stages (Cardenas and Felix, 2009). However, opioids are not recommended for use over prolonged periods because of the risk of addiction and therefore are of less use for chronic pain conditions (Wrigley and Sidall, 2007). The risk of opioid addiction is considered to be so high that it is now required that all opioids carry prominent warnings (BBC

News, 2019). Where neuropathic pain is concerned, the antidepressant Amitriptyline and the antiepileptics Pregabalin and Gabapentin are most effective but the literature is limited (Hagen and Rekand, 2015). All of these drugs can cause unpleasant side effects such as dizziness, dry mouth, increased spasticity, constipation and urinary retention, which increase with higher doses (Hagen and Rekand, 2015), and which can be particularly problematic for people with spinal cord injury who will already have bladder and bowel difficulties associated with their injury. In general neuropathic pain is refractory to pharmacological treatments (Burke, et al., 2017) and it is estimated that they only reduce 50% of the pain in approximately one-third of people (Siddall, 2009).

Non-pharmacological treatments are frequently used in both neuropathic and nociceptive pain conditions in spinal cord injury but research focusing on these approaches in the spinal cord injured population is even more limited than on drug treatments (Burke, et al., 2017). However some studies have found them to be of benefit. A recent study found that massage therapy reduced both pain and fatigue in people with SCI living in the community (Lovas et al., 2017) and cognitive behavioural treatment programmes have been found to improve quality of life (Nicholson Perry, Nicholas and Middleton, 2011) and reduce life interference from pain (Nicholson Perry, Nicholas and Middleton, 2010). Additionally, physiotherapy, exercise and acupuncture have had promising results (Heutink et al., 2011) but it remains that only a small number of people with spinal cord injury have access to these nonpharmacological treatment programs (Cardenas and Felix 2009). Adding to the treatment difficulties is that both nociceptive and neuropathic pain are likely to occur simultaneously, suggesting that the use of one type of treatment will not be sufficient in improving both kinds of pain (Hagen and Rekind, 2015). It is likely that treatment may need to target more precisely the different pain being experienced with various treatment options being considered.

When looking at treating pain and in studies focusing on pain, the outcome being targeted is important to consider. Many previous studies looking at pain in spinal cord injury have focused on pain intensity as the sole measure of

pain, and numeric rating scales have been recommended for use in assessing pain with SCI (Bryce, et al., 2007). However, as early as 1999 studies were suggesting that pain intensity alone was not a sufficient outcome measure because of the multidimensional complexity of the pain experience (Seres, 1999; Follett, 1999). More recently a greater interest in a wider range of pain-related outcomes has been emerging in the literature (Cuff, Fan, Bombardier, Graves, and Kalpakjian, 2014). One of these is the degree to which pain interferes with life activities. Pain interference has been associated with reduced engagement with household chores, work, exercise, sleep and social activities (Widerström-Noga, Felipe-Cuervo, Yezierski, 2001; Rintala, Loubser, Castro, Hart, Fuhrer, 1998), and additionally with quality of life more generally (Perry, Nicholas, and Middleton, 2009). Where depression following spinal cord injury is concerned, pain interference has been found to exert a greater influence than pain intensity, supporting the idea that a focus on pain intensity alone is not sufficient in reducing the risks of psychological disorders after spinal cord injury (Cuff et al., 2014). Treatment, therefore may need to be aimed at improving a range of pain-related outcomes.

The biopsychosocial model of pain acknowledges that pain may have an underlying biological cause, but it also suggests that psychological and social factors can have a profound effect on the pain experience and the individual's subsequent functioning (Widerström-Noga, Finnerup and Siddall, 2009). Therefore, research is needed that addresses each of these factors in an integrated manner, to see how they combine to maintain and aggravate pain for people with spinal cord injury. As a result of the research over the past few decades, theories of pain now tend to fall in to three broad categories; biological theories, psychological theories, and social theories. Each of these, along with specific biopsychosocial factors, will be discussed in the following chapters, focusing initially on the literature in the able bodied populations, where there is a greater number of studies, and then specifically in spinal cord injury. Many of the theoretical models have not been tested on the SCI pain population specifically, so applying them here needs to be done with caution. However, by analyzing a wide range of biopsychosocial factors it may be possible to get an indication of which models might be relevant to people with

pain and SCI. This is explored further in the ‘Discussion’ section where the models that appear supported by the results are highlighted.

5 Chapter 3 - Biological Theories of Pain

Specificity Theory and Pattern Theory remained dominant in the theoretical concept of pain for decades. However, Melzack and Wall (1965) identified certain weaknesses inherent within them. The theories could not explain the phenomenon of phantom limb symptoms, where an individual experiences painful sensations, itching or tingling in the missing limb. With phantom limb pain, pain occurs without a stimulus, therefore pain signals are not travelling via a direct line of transmission from the site of injury to the brain. This is supported by the fact that treatments that involved lesions of the Central Nervous System and the Peripheral Nervous System did not remove phantom limb pain permanently, once again casting doubt on the idea of a direct line of transmission of pain signals to the brain (Melzack and Wall, 1965). Extreme phantom limb pain can be triggered by just a gentle touch on another part of the body suggesting that there is not always a direct relationship between the severity of the injury and the intensity of the pain experience. Melzack and Wall (1965) provided further evidence of this citing Beecher (1946) who documented that US soldiers, when severely wounded on the battle field, denied having any pain from those wounds. This suggests that pain is more complex than these theories propose and that other factors must be involved. Therefore contemporary biological theories of pain will be discussed, followed by an analysis of the role of cortisol in the pain experience.

5.1 The Gate Control Theory of Pain

The Gate Control Theory (Melzack and Wall, 1965) attempted to explain how psychological variables were involved in the physiological sensation of pain. This can be seen in Figure 5. It suggests that a mechanism in the dorsal horn of the spine acts as a gate to pain. The gate can be opened and closed by bottom-up processes from the location of the physical damage and by top-

down processes triggered by cognitions and emotions. When the gate is open the pain intensity will be greater. According to the theory, the three types of nociceptors previously discussed are involved; two small diameter neurons and a large diameter neuron. The small diameter neurons are the myelinated Aδ fibres, which carry information about sharp pain related to tissue damage, and unmyelinated slower conducting C polymodal fibres, which carry information about dull, throbbing pain. These carry information to the substantia gelatinosa in the dorsal horn of the spine where they trigger the release of the neurotransmitter Substance P. These both open the gate and activate the transmitter fibres which carry the pain information to the brain via the spinothalamic tract. Large diameter neurons, the Aβ fibres, respond to gentle touch, such as gently rubbing an area that has been hurt, and these send information to the dorsal horn more quickly than C polymodal fibres. This reduces the amount of activation of the transmission cells so that they fail to reach a critical threshold, closing the gate and reducing the pain experience (Melzack and Wall, 1965).

When the gate is open and transmitter fibres are activated, information from Aδ fibres is sent via the thalamus on to areas of the cortex where actions can be initiated to remove the damaged body part from the noxious stimulus. Information from C polymodal fibres is sent to the limbic system, hypothalamus and the autonomic nervous system (ANS), which triggers an emotional response and activates the ANS. This neural activity is sent back down to the gate via reticulospinal fibres and can either open or close the gate. Emotional responses such as feeling relaxed and unconcerned about the pain increase the release of endorphins, closing the gate and reducing pain intensity. Responses such as catastrophising, worrying and feeling anxious about the pain, decrease the release of endorphins, opening the gate and increasing the pain experience (Melzack and Wall, 1965).

At its introduction the Gate Control Theory was quite well supported, and it is still considered to have been importantly influential in pain research (Sufka and Price, 2002; Mendell, 2014). However, although the general ideas contained within it provide an acceptable account of the mechanisms of pain,

(Sufka and Price, 2002), it is inaccurate in its detail. For example, it is known that other gating mechanisms exist such as an opioid-dependent gate which is opened and closed by the presence of opiates such as endorphins (Mendell, 2014). Additionally, it has also been found that neural activity in the dorsal horn is far more complex than Melzack and Wall (1965) reported (Mendell, 2014). Like the Specificity and Pattern theories, the Gate Control Theory still assumes that the pain process begins at the site of an injury and, therefore, it cannot fully explain certain chronic pain problems that have no known pathological cause, or neuropathic pain problems such as phantom limb and spinal cord injury pain (Moayedi and Davis, 2013).

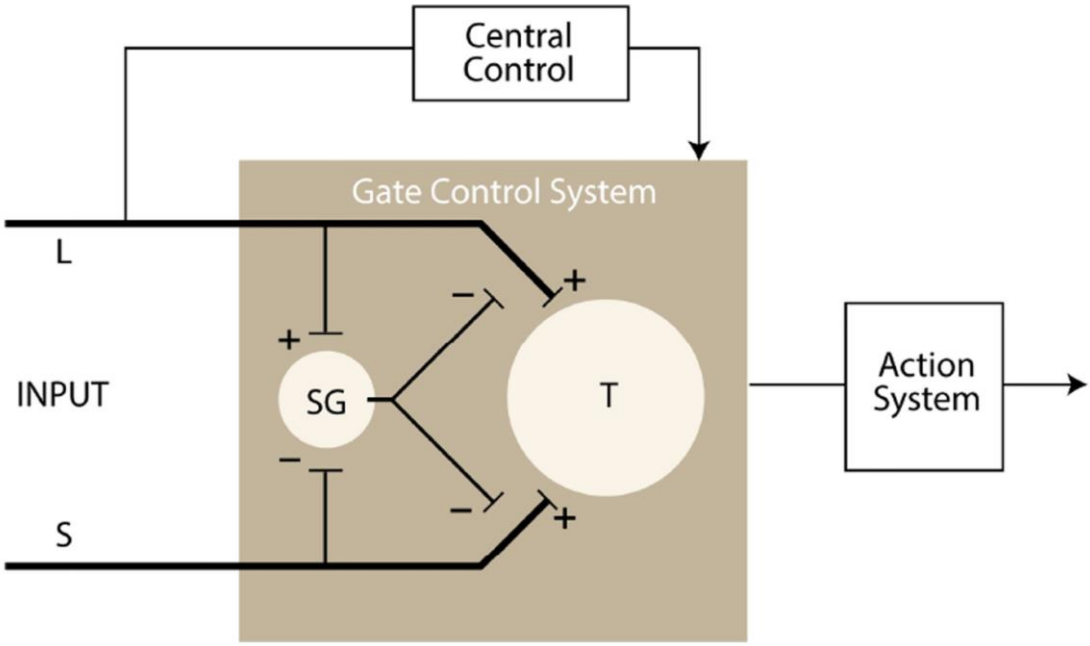

Figure 5. Schematic diagram of the gate control theory of pain mechanisms: L, the large-diameter fibers; S, the small-diameter fibers. The fibers project to the substantia gelatinosa (SG) and first central transmission (T) cells. The inhibitory effect exerted by SG on the afferent fiber terminals is increased by activity in L fibers and decreased by activity in S fibers. The central control trigger is represented by a line running from the large-fiber system to the central control mechanisms; these mechanisms, in turn, project back to the gate control system. The T cells project to the entry cells of the action system. + = Excitation; — = inhibition. From “Pain Mechanisms: A New Theory” by R. Melzack, and P. D. Wall, 1965. *Science, 150*, p. 975.

5.2 The Neuromatrix Theory of Pain

In response to the problems identified with the Gate Control Theory, Melzack (1993) proposed a Neuromatrix Theory of pain (Figure 6), which suggests that the brain is able to perceive pain in the absence of external stimuli. This perception is modulated by sensory inputs but not caused by them. According to the theory, the neuromatrix consists of a widespread network of neurons, incorporating many areas of the brain, processing and synthesising information, generating patterns and producing the pattern that we feel as our whole body and producing awareness and action (Melzack, 1993). More specifically, Melzack (1993) describes the neuromatrix as a genetically determined network of neurons with loops between the thalamus and cortex and the cortex and limbic system.

The neuromatrix has four components. Firstly there is the body-self neuromatrix itself, the network of neurons from which the body-self perception grows. Secondly, there are cyclical and parallel processing and synthesis of nerve impulses via the thalamus and cortex loop and the cortex and limbic system loop. This produces a characteristic pattern, that Melzack (1993) refers to as the neurosignature, and which is stamped on all neural impulses flowing through it. It is produced by the processing and synthesis of nerve impulses in the neuromatrix and then imparted on the nerve impulses that flow through the neuromatrix. In this way it is both genetically determined and also shaped by experience. Thirdly, the neurosignature, the pattern of nerve impulses of the neuromatrix, is converted into a flow of awareness by the ‘sentient neural hub’, which represents different areas of the brain. Lastly, the neurosignature can also activate an action neuromatrix, which in turn switches on neurons in the spinal cord to produce movement. In this way the neuromatrix divides, with one pattern flowing through the sentient neural hub to create the experience or awareness, another activating neurons to produce movement, whilst a third is directed at homeostatic regulation, such as autonomic and endocrine regulation. These occur concurrently and sensations such as pain or fatigue are produced by the neurosignature, without input from limbs or proprioceptive feedback and so might explain the

phantom limb phenomena (Melzack, 1993). Where phantom limb or neuropathic pain is concerned the action neuromatrix might be sending out ever stronger messages to move the limb. When this does not happen it results in the experience of shooting pains or muscle cramps caused by abnormal patterns generated by the action neuromatrix (Melzack,1993).

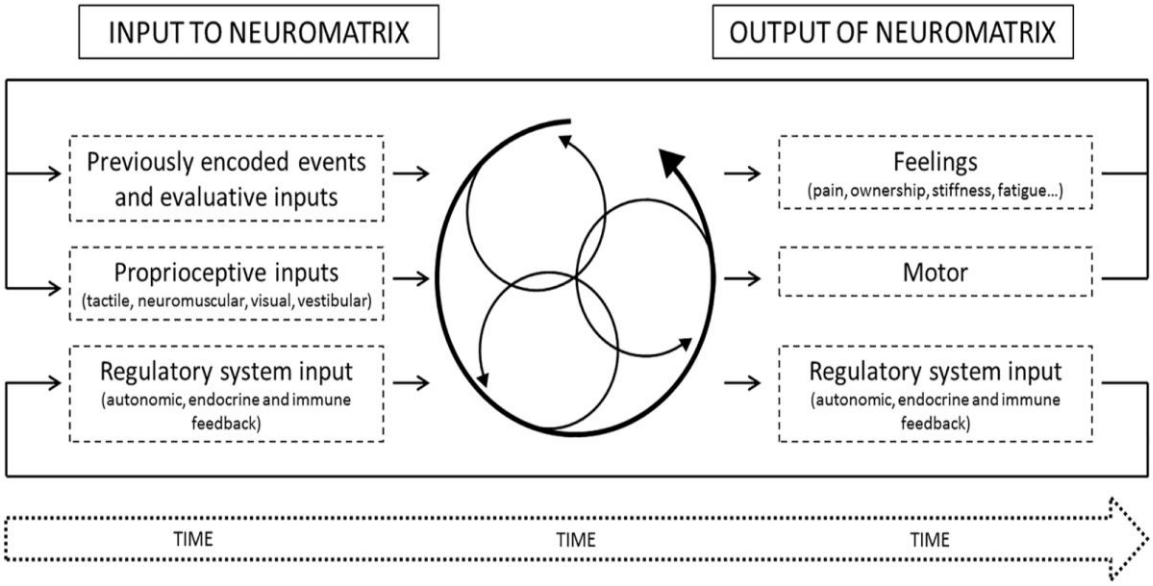

Figure 6. Factors that contribute to the patterns of activity generated by the body-self neuromatrix, which is comprised of sensory (S), affective (A), and cognitive (C) neuromodules. The output patterns from the neuromatrix produce the multiple dimensions of pain experience, as well as concurrent homeostatic and behavioral responses. From "Evolution of the Neuromatrix Theory of Pain. The Prithvi Raj Lecture: Presented at the Third World Congress of World Institute of Pain, Barcelona 2004," by R. Melzack, 2005, *Pain Practice, 5*(2), p. 91. Copyright 2005 by Blackwell Publishing Ltd. With permission.

The neuromatrix theory is thought to have advanced understanding of pain conditions considerably but it has been criticised as being mainly conceptual as few specific neuroanatomical structures have been identified (Belan, Wallwork, Gallace, Spence, and Moseley, 2017). However, support for the neuromatrix, or at least aspects of it, come from studies on rats. Coderre, Vaccarino and Melzack (1990) used the formalin pain test, an injection that produces intense pain for the first five minutes and which is followed about 15 minutes later by further pain. They found that an anaesthetic would only block the late pain completely if it was administered before the onset of the early

pain. If it was given after the early pain the rat would still experience the later pain. This suggests that the later pain was not only produced by sensory information, but also by neural processes or patterns that already exist. Whilst this doesn't provide evidence for the existence of a neuromatrix as theorised by Melzack (1993), it does support the principle that the experience of pain is not solely a result of sensory stimulation.

5.3 Biological Factors of Pain: Cortisol and the Stress Response

Human beings depend on biological equilibrium or homeostasis, a stable state, to remain healthy. Challenges to homeostasis can come from within the body, for example in the form of anxiety, or from external sources such as a threat to safety. Selye (1936) was the first person to use the word 'stress' as a term for such challenges. Stress, therefore, is defined in this context as "a state of disharmony, or threatened homeostasis" (Chrousos and Gold, 1992, p. 1245). Selye proposed that when threats (or perceived threats) to homeostasis occur, individuals use what he referred to as 'adaptational responses'. These are the mental and physical efforts employed to return the body to a stable state. In acute and/or mild cases of stress, adaptational responses work well to maintain equilibrium but Selye suggested that chronic or severe stress depletes adaptational responses until a state of exhaustion occurs, and this is when stress can lead to illness. Selye termed this state the 'General Adaptation Syndrome" (Selye, 1936). This link between chronic stress and ill health has since been well established, (e.g. Chida and Steptoe, 2008; Prior et al., 2016).

Recently, the importance of perceived stress and the stress response system in the process of pain has been proposed and it has been suggested that both psychological stress and physical stress from injury or infection are important and disrupt homeostasis (Melzack, 2005). Once this has happened the stress system is activated in order to reinstate the equilibrium. An important part of this process is the release of cortisol which, it has been speculated, may have a significant role in the experience of chronic pain (Melzack, 2005). Cortisol is

a corticosteroid hormone, one of the glucocorticoid group, that has pleiotropic effects, such as regulating immune and cardiovascular responses and behavioural processes (Nicolaides, Kyratzi, Lamprokostopoulou, Chrousos, and Charmandari, 2015), and reducing inflammation to prevent tissue and nerve damage (Hannibal and Bishop, 2014). The release of cortisol follows a particular diurnal pattern (see Figure 7), with cortisol levels increasing just prior to wakening, and higher levels being released immediately upon waking for approximately 45 minutes to aid arousal, which is known as the cortisol awakening response (CAR; Pruessner et al., 1997; Stalder et al., 2016). This declines as the day continues and levels out later in the afternoon and evening, remaining stable during the night (Weitzman et al., 1971). It should be noted that individual differences exist in the levels of cortisol released and the diurnal pattern displayed, with some people exhibiting a much flatter pattern than others (Smythe et al., 1997). This can make patterning difficult to benchmark (Smythe et al., 1997).

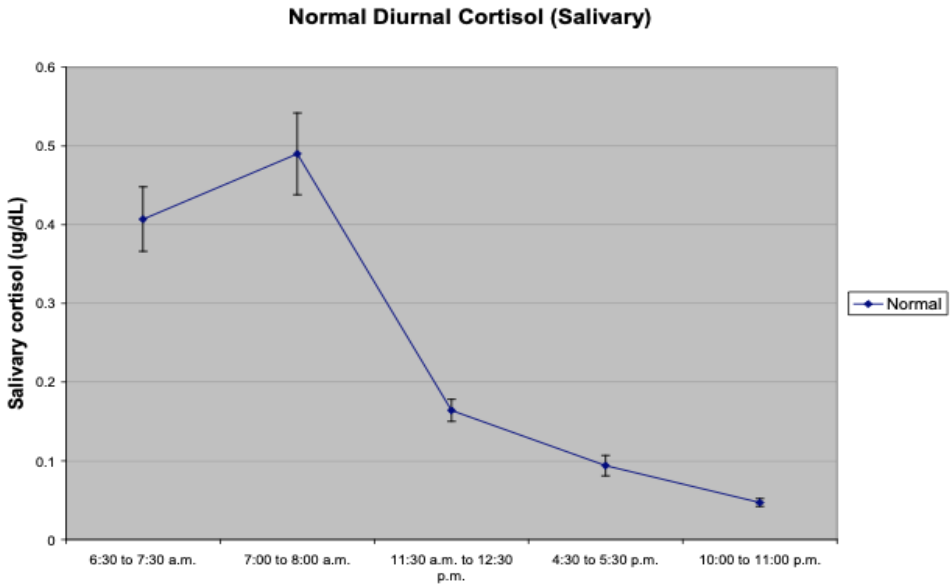

Figure 7 Cortisol diurnal pattern. Cortisol secretion is higher and continues to increase upon wakening, then drops off as the day progresses, stabilising during late afternoon and over night. From “High Sensitivity Salivary Cortisol Immunoassay Kit,” by *Salimetrics*, 2011. Copyright 2011 by Salimetrics Europe Ltd.

During the day cortisol provides energy to the neuromuscular system and brain by maintaining blood glucose levels (Hannibal and Bishop, 2014). The CAR is distinct from and unrelated to cortisol produced at other times of the day (Maina, Palmas, Bovenzi and Filon, 2009) and to cortisol produced when psychological stress is induced experimentally (Bouma, Riese, Ormel, Verhulst, and Oldehinkel, 2009). Therefore, it is not a reliable biomarker of changes caused by stress or as an indication of HPA axis activity (Clow, Hucklebridge, Stalder, Evans, and Thorn, 2010). Measures of cortisol produced at other times of day might better reflect such changes.

As well as having a homeostatic role, cortisol is produced by the adrenal cortex as part of the HPA axis stress response (Nicolaides et al., 2015). When an individual experiences psychological stress or physical injury, the information arrives at the amygdala's basolateral nucleus where it is processed and sent to the central nucleus of the amygdala. The amygdala initiates an immediate sympathetic response, releasing noradrenaline and adrenaline to, for example, increase blood pressure and heart rate, and this also functions as a pro inflammatory response to destroy any pathogens etc. (Hannibal and Bishop, 2014). Activation of the amygdala additionally sends a delayed message to the bed nucleus of the stria terminalis in the basal forebrain and neurons here activate the HPA axis.

The process of the HPA axis can be seen in Figure 8. Firstly, parvocellular neurosecretary cells, small neurons in the paraventricular nuclei of the hypothalamus (PVN), secrete arginine vasopressin (AVP), a neuropeptide hormone. This stimulates the release of corticotropin-releasing factor (CRF) into the hypothalamo-pituitary portal circulation (blood vessels connecting the hypothalamus with the pituitary gland). CRF binds to CRF type 1 receptors (CRFR1) on the surface of pituitary cells of the anterior pituitary gland and activates the cyclic adenosine monophosphate pathway (cAMP), aided by the secondary messengers inositol triphosphate (IP3) and diacylglycerol (DAG), which relay and amplify the strength of signals. This can either start or stop the secretion of adrenocorticotropic hormone (ACTH) via the vasopressin V1B receptor. ACTH travels in the bloodstream to the adrenal cortex, binding to the

melanocortin type 2 receptor (MC2-R), where cortisol is released. The release of glucocorticoids is generally an adaptive response to stress, but both excessive or reduced HPA activity can be problematic, as discussed later in this chapter. To manage this, cortisol travels to the brain through the bloodstream where low affinity glucocorticoid receptors respond by inhibiting further release of CRF when cortisol levels are high, thus preventing further cortisol production. This is referred to as the glucocorticoid negative feedback system, which has an important regulatory role in managing the duration and amount of HPA activity and the resulting cortisol secretion (Smith and Vale, 2006). Glucocorticoid receptors are thought to be located in many areas of the brain, but it is thought that those in the hippocampus (Jacobson and Sapolsky, 1991) and paraventricular nucleus of the hypothalamus (Sawchenko, 1987) are particularly important with regard to this negative feedback system.

When operating normally, the HPA axis and cortisol specifically, have an important anti-inflammatory role that aids stress management and limits the spread of pain. However, if the level of threat associated with pain is high, this can result in an increased stress response and dysregulation of cortisol production (Carlesso, Sturgeon and Zautra, 2016). Higher cortisol levels have been consistently associated with chronic pain conditions and negative life events, as well as long-term stress, and these results tend to have medium or large effect sizes reflecting the close association between elevated cortisol and stressful life periods (Staufenbiel, Penninx, Spijker, Elzinga and van Rossum, 2012).

Few studies have examined the association between perceived stress and pain intensity and pain interference with daily activities, however higher stress has been associated with both, with the association with pain interference maintaining even when pain intensity was controlled for (White, Jiang, Hall, Katz, and Zimmerman, 2015). However, pain has been associated with both hypercortisolism (Coloca and Benedetti, 2007) and hypocortisolism (Fries, Hesse, Hellhammer and Hellhammer, 2005). Hypercortisolism, characterised by increased and prolonged cortisol secretion, can be caused by stressors such as acute pain, which elicits higher cortisol production. A maladaptive

response to the pain can lead to ongoing and magnified cortisol secretion which exhausts cortisol levels, resulting in hypocortisolism, which can be represented either by low levels of cortisol secretion or by a flattened diurnal cortisol pattern, and this could mark the transition from acute to chronic pain (Hannibal and Bishop, 2014).

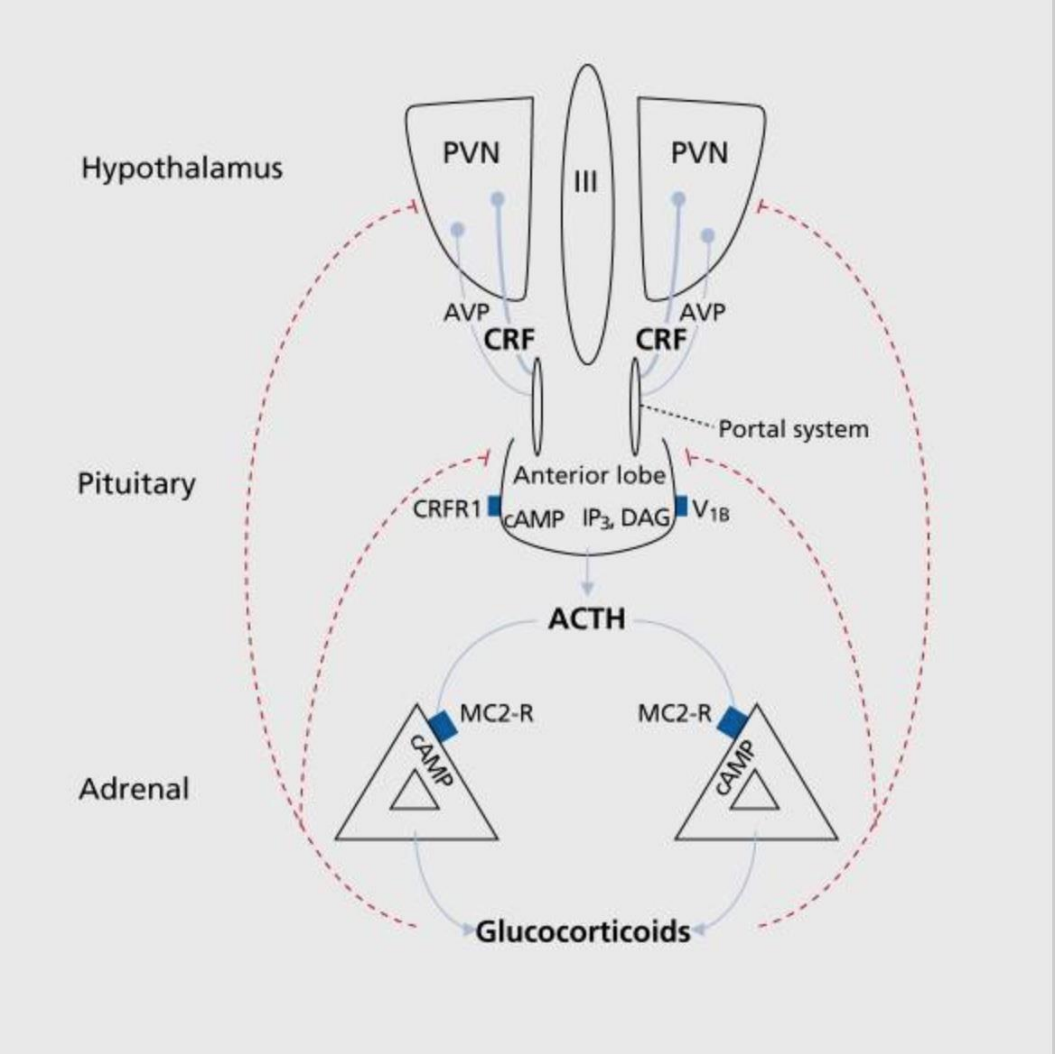

Figure 8. Schematic representation of the HPA (HPA) axis. See text for description. PVN = Paraventricular nucleus; AVP = Arginine vasopressin; CRF = Corticotropin-releasing factor; CRFR1 = CRF type 1 receptors; cAMP = Cyclic adenosine monophosphate pathway; ACTH = Adrenocorticotropic hormone; MC2-R = Melanocortin type 2 receptor; IP3 = Inositol triphosphate; DAG = Diacylglycerol. From "The Role of the HPA Axis in the Neuroendocrine Responses to Stress," by S. M. Smith and W. W. Vale, 2006, *Dialogues in Clinical Neuroscience*, *8*(4), p. 384. Copyright 2006 by LLS SAS.

This demonstrates that cortisol secretion that is either too high or too low can

both be problematic. Inappropriate regulation of the stress response has consistently been associated with poor health, particularly cardiovascular disease (Chrousos, 2009). However, it has also been associated with the development of other acute and chronic conditions such as autoimmune disorders (Chrousos, 2000), allergic conditions (Chrousos, 2009), gastrointestinal symptoms (Nicolaides et al., 2015), and psychiatric conditions (Chrousos and Kino, 2007). It has now also been linked to chronic pain (Melzack, 2005) because if cortisol production is excessive or prolonged it can lead to damage to bone, neural tissue and muscle and produce feelings of weakness and fatigue (McEwen, 2002). This is because after injury cortisol activates the production of glucose in high levels by breaking down the protein in muscles and preventing calcium replacement in bone (Chrousos and Gold, 1992). Sustained release of cortisol can also suppress the immune system (Nicolaides et al, 2015) and has been associated with the disruption of the feedback system, which inhibits the release of CRF (Fries et al., 2005). Activation and disinhibition of CRF is problematic because it causes the release of the proinflammatory neurotransmitter noradrenaline and inflammation is associated with many chronic health conditions including pain (Tak, et al., 2011).

CRF is found in a number of regions in the brain and CRF activation in the amygdala has been associated with the experience of pain when tissue damage is absent (Ji, Fu, Adwaniker, and Neugebauer, 2013). It is thought that the amygdala may be associated with chronic pain through prolonged cortisol production, which has a conditioning effect on it by forming fear-based memories (de Quervain, Schwabe, and Roozendaal, 2017). Activation of the HPA axis is then increased as a conditioned stress response (Colloca and Benedetti, 2007). Figure 9 demonstrates how this might result in the transition from acute to chronic pain, with a maladaptive response to pain resulting in prolonged activation of the HPA axis, cortisol dysfunction, increased inflammation and a conditioned fear-based memory (Hannibal and Bishop, 2014).

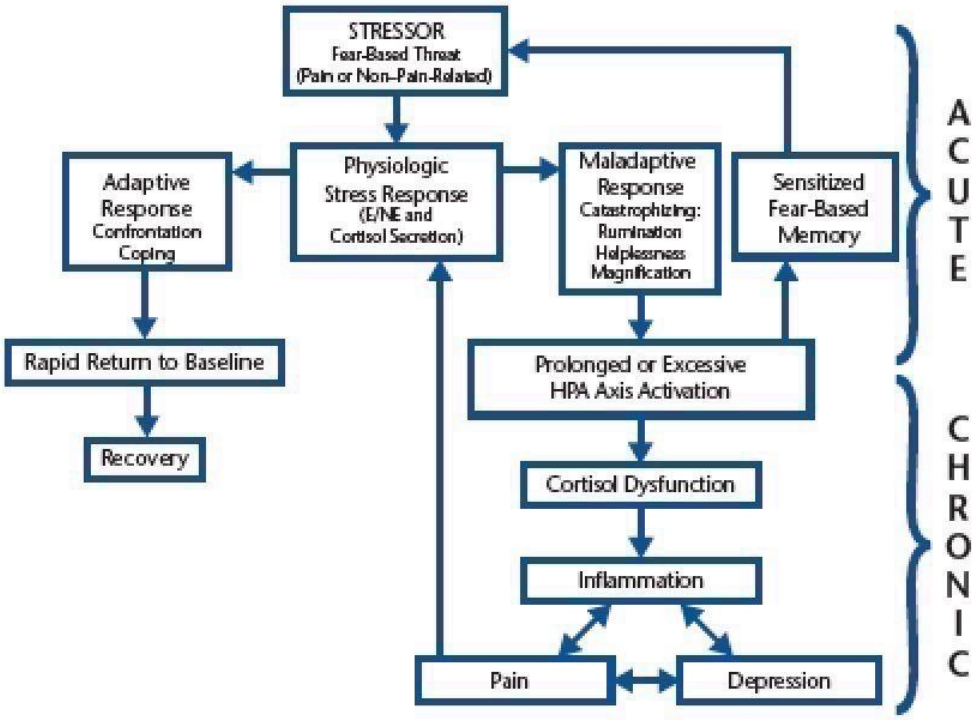

Figure 9. Proposed role of stress-related HPA axis activation in the transition from acute to chronic pain. Acute stress response: pain or non–pain-related stressor activates a normal physiologic stress response (short-term sympathetic release of epinepherine and norepinepherine [E/NE] followed by secretion of the anti-inflammatory hormone, cortisol). An adaptive coping response permits the return to normal levels of E/NE, cortisol, and inflammation; a maladaptive response causes excessive or prolonged cortisol secretion and creates a fear-based memory of the stressful stimulus that is sensitized and readily reactivated by future stressors. Chronic stress response: prolonged cortisol secretion (due to maladaptive coping response to acute stress) results in cortisol dysfunction. Cortisol dysfunction results in unmodulated inflammation following reactivation of the stress response, which may contribute to a cycle of inflammation, depression, and pain; pain is a stressor that may reactivate a proinflammatory stress response, now unmodulated due to cortisol dysfunction. From “Chronic stress, Cortisol Dysfunction, and Pain: A Psychoneuroendocrine Rationale for Stress Management in Pain Rehabilitation,” by K. E. Hannibal and M. D. Bishop, 2014, *Physical Therapy, 94*(12), p. 1821. Copyright 2014 by American Physical Therapy Association.

Areas of the brain such as the amygdala and the hippocampus that are involved in the neural circuitry of the HPA axis are also implicated in the modulation of pain. This could result in increased pain sensitivity as a non-painful stimulus activates the pain neural network (Zouikr and Karshikoff, 2017). Although this suggests that activity of the HPA axis might contribute to

pain, it is not clear precisely what role cortisol has in modulating this. It is likely that following a physical injury, healing begins through the secretion of proinflammatory cytokines which also serve to reduce pain (Hannibal and Bishop, 2014). However, if stress is high and causing hypocortisolism, cortisol will no longer have its inhibitory effect and the inflammatory response will be prolonged, resulting in impaired healing and higher pain sensitivity (Fries et al., 2005). Therefore, whilst cortisol on its own may not be sufficient to cause pain conditions, cortisol release could be influenced by other factors such as psychological stress and genetic predispositions (Melzack, 2005). These factors together could produce the problems of chronic pain. This is supported by evidence from Chrousos and Gold (1992) who propose that chronic fatigue syndrome, rheumatoid arthritis and fibromyalgia can all be caused by a dysfunction of the stress system causing muscle tissue atrophy and decalcification of bone and leading to myopathy, weakness and fatigue. Research focusing on how cortisol interacts with other psychosocial variables to impact on pain outcomes is therefore important.

The relationship between stress and the HPA axis response is not a straightforward one, with stress having the capability of both increasing and decreasing activity, and this is reflected in the differing results found in the literature. The resulting hypercortisolism and hypocortisolism might be explained by the different types of stressors involved and the different characteristics of the individual (Miller, Chen and Zhou, 2007). Cortisol secretion that has a high but flat diurnal pattern has been associated with stressors that are traumatic or represent a physical threat, stressors that cannot be controlled, and stress associated with loss (Miller et al., 2007). However, where individual characteristics are concerned, people who develop depression following a trauma show increased cortisol levels, whereas people who develop post-traumatic stress disorder (PTSD) following a stressful traumatic occurrence have a lower daily cortisol secretion (Miller et al., 2007). This suggests that stress does not act in isolation with regard to HPA activity but will be moderated by other psychological variables and by the type of stress being experienced. This in turn will have different implications for health, depending on whether hypercortisolism or hypocortisolism is triggered.

5.3.1 Cortisol and Psychopathology

One area of interest that has received a lot of attention is the relationship between cortisol and psychopathology. There is evidence that stress exacerbates pain on a momentary basis and the same has been found for cortisol secretion. Pain, however, has not always been found to predict stress levels although it has been associated with it on a moment-by-moment basis (Fischer et al., 2016). It might be that rather than causing stress, pain is more likely to cause distress in the form of anxiety or depression (Okifuji, Bradshaw, Donaldson, & Turk, 2011). It has been suggested that some psychiatric disorders, particularly depression and anxiety, could develop as a result of the dysregulation of the HPA axis (Vreeburg et al., 2010).

There is a well-established relationship between stressful life events and depression, which becomes stronger with each depressive episode (Morris, Ciesla, & Garber, 2010). The HPA axis has been linked to a vulnerability for depression (Oldehinkel & Bouma, 2011) therefore the association could be caused by changes in reactivity of this system. Additionally, major depressive disorder (MDD) has been associated with a reduced response from the HPA axis to feedback from glucocorticoids (Carroll, 1982). The resulting prolonged release of cortisol has been found to result in MDD in some cases (Lewis & Smith, 1983). Supporting this idea is the finding that each depressive episode leads to elevated cortisol levels during remission (Bos et al., 2005). This study found that high cortisol reactivity to low-level stressors was predictive of future depressive symptoms, suggesting that individual differences in HPA functioning could indicate those most at risk of recurrent depressive episodes (Bos et al., 2005). However, MDD has also been linked to a reduction in cortisol secretion over longer periods of time and it is possible that it causes changes in the endocrine system (Steudte-Schmiedgen et al., 2017).

More specifically, elevated morning levels of cortisol (Goodyer, Herbert, Tamplin, & Altham, 2000), and elevated evening levels of cortisol have been associated with MDD (Harris et al., 2000), the latter having been found in 50%

of patients with depression (O'Brian et al., 2004). A heightened CAR (CAR) is predictive of future major depressive episodes, both as a recurrence and as a first onset, over a two and a half year period, independently of major stressful life events (Vrshek-Schallhorn, 2013). However, the effect is stronger for predicting a recurrence when a history of depression is present, than for first onset. It is therefore possible that elevated CAR has trait-like characteristics (Cowen, 2010). Even when individuals have no history themselves of depression, they still show a high waking salivary response if they have a parental history of depression, or if they score highly for neuroticism. Both of these factors place them at greater risk of future depressive episodes (Mannie, Harmer & Cowen, 2007). A higher CAR has also been associated with a key personality trait that has been closely linked to depression: hopelessness reactivity (van Santen et al., 2011), providing further support for the idea that HPA axis dysregulation may represent a trait vulnerability for depression.

Given that the CAR has a significant genetic component (Wüst, Federenko, Hellhammer, & Kirschbaum, 2000), this may also be the case for psychological disorders such as anxiety (Adam et al., 2014). It has been suggested, for example, that panic disorder and PTSD might be preceded by a blunted cortisol response to stress and hypocortisolism respectively (Wintermann, Kirschbaum, & Petrowski, 2016). This down-regulated HPA activity might reflect poor adaptive responses to stress and poor coping strategies, leading to a greater risk of these two anxiety disorders (Wintermann, et al., 2016). Alternatively, it could reflect an underlying neurobiological trait that results in both changes to cortisol secretion and risk of psychological difficulties (Adam et al., 2014). A diathesis stress approach demonstrates how these different explanations might be combined (as shown in Figure 10; Tafet & Nemeroff, 2016). This hypothesis suggests that a central nervous system (CNS) phenotype and cognitive vulnerability results from the combination of genetic inheritance, early life stress and later chronic stress.

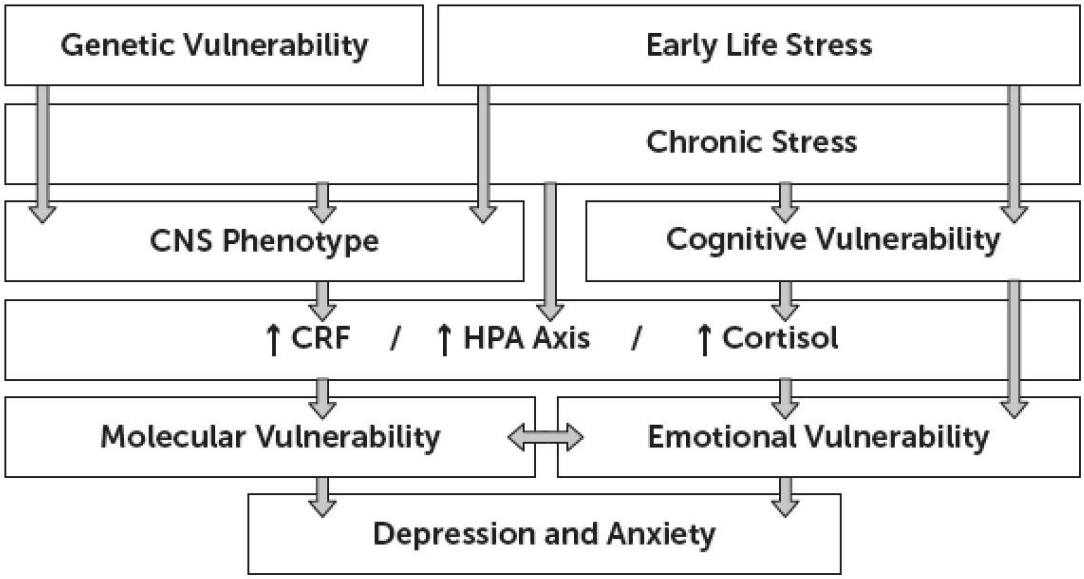

Figure 10. Schematic representation of different factors involved in the stress response and their potential role in stress and depression. Genetic polymorphisms (represented as genetic vulnerability) participate in the development of the CNS and, together with the influence of early environmental factors (represented by early life stress) and chronic stress, result in a particular CNS phenotype. Early life stress may also induce certain cognitive vulnerability, which in turn may result in emotional vulnerability. Upon the impact of traumatic events or chronic stress, a predisposed CNS responds with increased levels of CRF, hyperactivation of the HPA axis, and increased levels of cortisol, which may lead to molecular changes in different circuits (represented by molecular vulnerability), as well as altered cognitive and emotional responses (represented by emotional vulnerability). This, in turn, may result in increased vulnerability for the development of symptoms of anxiety and depression. CRF, corticotropin-releasing factor; HPA, HPA. From "The Links Between Stress and Depression: Psychoneuroendocrinological, Genetic, and Environmental Interactions," by G. E. Tafet & C. B. Nemeroff, 2016, *The Journal of Neuropsychiatry and Clinical Neurosciences, 28,* p. 86. Copyright 2016 by the American Neuropsychiatric Association.

Cognitive vulnerability may lead to emotional vulnerability, and cognitive vulnerability with the CNS phenotype might result in increases in cortisol secretion, CRF levels and HPA axis activity, leading to further emotional vulnerability and changes in molecular structures. This then leads to an increased risk of developing anxiety and mood disorders (Tafet & Nemeroff, 2016). In this way, a genetic predisposition, coupled with early and recent stressors, cause changes in structures such as the amygdala and hippocampus, and in psychological processing, leading to greater vulnerability

for psychological problems (Tafet & Nemeroff, 2016).

However, the literature is inconsistent where cortisol and psychopathology are concerned, especially with regards to the CAR (CAR). Some studies report a higher CAR in those at risk of MDD (Engert, Efanov, Dedovic, Dagher, & Pruessner, 2011) or in those with a MDD diagnosis (Bhagwagar, Hafizi, & Cowen, 2005), whereas others report a lower CAR in both of these groups (Dedovic et al., 2010). As with depression, it is not clear whether anxiety is associated with an elevated CAR, a lower CAR or to a flattened diurnal cortisol rhythm more generally. A recent review suggested that there is not a strong relationship between HPA axis dysregulation and anxiety disorders (Elnazar & Baldwin, 2014), however, a strong association has been found between increased CAR and anxiety in comparison to people who had never had anxiety or who were remitted (Vreeburg et al., 2010).

It is likely that this comes back to the issues of hypercortisolism, caused by acute stress, verses hypocortisolim, related to on-going chronic stress (Fries et al., 2005). In a similar way, studies focusing mainly on acute anxiety have found an elevated CAR, (Vreeburg et al., 2010; Mantella et al., 2008), whereas those concerned with a sample of people with chronic anxiety have found a significantly lower CAR than people without anxiety (Hek et al., 2013). This supports a review of cortisol and its associations with stress and mental health which reports differences in the findings concerning whether anxiety is associated with an increase, decrease or no change in cortisol levels (Staufenbiel et al., 2012). This could reflect the nature of anxiety disorders. Lower hair cortisol has been found in patients with GAD compared to healthy controls (Steudte et al., 2011). GAD is characterized by chronic worry and anxiety about general day-to-day issues. This long-term worry might result in hypocortisolism compared to more acute anxiety disorders, which could see an initial cortisol increase.

The pattern of cortisol secretion in people with posttraumatic stress disorder (PTSD) supports this notion. Soon after a traumatic event, cortisol has been found to be high, whereas some months later a decrease can be seen (Luo et

al, 2012). These results have been supported in a recent meta-analysis of cortisol research, where both GAD and PTSD were associated with a 17% lower hair cortisol concentration (Stalder et al., 2017). Miller, Chen and Zhou (2007) have hypothesized that a trauma causes a rise in cortisol as part of the stress response in dealing with the stressor. This is followed over time by a decrease in cortisol to below the baseline. Therefore, it is possible that the different results reported by Staufenbiel et al. (2012) reflect the different phases of anxiety and of trauma processing. As with stress, a down-regulation of the HPA axis may result from long-term chronic anxiety conditions. This supports the possibility of two pathways concerning morning cortisol levels: a high CAR might represent a genetic vulnerability for certain psychological disorders, whereas a low CAR and chronic mental ill-health might result from high and on-going allostatic load (Vreeburg et al., 2013). Allostatic load is defined as the wear and tear on the body resulting from prolonged exposure to stress. Where SCI is concerned, it might then be expected that cortisol levels would increase immediately following the trauma, but reduce to below baseline over time alongside the chronicity of the injury.

Various associations between the diurnal cortisol rhythm more generally and anxiety and depression have also been found, for example, a flattened, unresponsive pattern of cortisol activity, with lower morning cortisol and higher afternoon cortisol levels has been found to have a stronger association with depression than CAR (Burke, Davis, Otte & Mohr, 2005). This, combined with impaired stress recovery was particularly associated with depression in older and more severely depressed individuals (Burke, Davis, Otte & Mohr, 2005). In support of this, more recently the CAR was not associated with the course of major depressive disorder in older adults, however, evening cortisol levels, associated with lower cortisol concentrations, predicted a poorer course (Kabia, Rhebergen, van Exel, Stek, & Comijs, 2016). The differences in cortisol secretion at different times of day and its relation to mental health has been seen longitudinally for both depression and anxiety. Over a two-year period, the CAR was found to be influential, with a lower CAR predicting a poorer, chronic course trajectory of both anxiety and mood disorders. Cortisol levels in the evening, however, were not associated with long-term trajectories

(Vreeburg et al., 2013). A possible explanation for these conflicting results might be that distress reflects a pattern of change in cortisol levels across the diurnal rhythm rather than in absolute levels at single time points (Vedhara, et al., 2003). This is supported by Stalder et al. (2016) who highlight that the CAR is not related to the production of cortisol at other times of the day and that as such it is not a reliable biomarker of changes caused by stress or as an indication of HPA (HPA) axis activity (Clow, Hucklebridge, Stalder, Evans, & Thorn, 2010).

It is likely that these differences stem from the fact that the precise interaction between cortisol and depression is not fully understood (Herbert, 2013). Glucocorticoids act on various neurological systems associated with mood and the HPA axis, and different types of depression have different effects, with melancholic depression resulting in heightened HPA activity and atypical depression resulting in a reduced stress response (Nicolaides et al., 2015). Similarly, chronic depression has been more closely associated with a blunted stress response whilst acute symptoms have been linked to higher cortisol secretion (Booij, Bouma, De Jonge, Ormel, & Oldehinkel, 2013). Some research has linked increased CRF, (which responds to alterations in cortisol) in the amygdala, to increased anxiety (Britton, Koob, Rivier & Vale, 1982) and it has been suggested that CRF in the amygdala may interact with cortisol during episodes of MDD or following a negative life event that precedes an episode of depression (Bao & Swaab, 2010).

Glucocorticoids are also closely involved in immune system functioning (Herbert, 2013) and reduced immune system functioning has been linked to MDD with higher levels of pro inflammatory cytokines (which have a role in regulating immune system functioning) found in the blood (Dowlati et al, 2010), although less research has been carried out in this area. The two-way relationship between cortisol and cytokines may provide a partial explanation for this. HPA activity is stimulated by cytokines but the pro-inflammatory activity of some cytokines may be reduced by cortisol. It is possible that the balance of this relationship can change, with either one or the other dominating (van der Meer, Hermus, Pesman, & Sweep, 1996), resulting in

inconsistencies in the precise nature of the relationship between cortisol and depression.

The lack of clarity concerning the association between cortisol and depression may also stem from the possibility that the population being studied is not a homogenous group. Research has consistently found that the link between depression and an increased risk of physical conditions such as diabetes and coronary heart disease is mediated by HPA hyperactivity (Cowen, 2010). However, HPA hyperactivity and the resulting elevated cortisol levels vary quite considerably across different patient groups, for example, between younger out-patient groups and older in-patient groups, with the latter having much bigger cortisol differences between depressed and non-depressed participants (Stetler, & Miller, 2011).

A strong association between anxiety and the cortisol diurnal rhythm has also been found in older adults. Those with GAD (GAD) had higher peak morning cortisol levels and higher overall cortisol levels than older adults without GAD. Higher cortisol was also positively associated with symptom severity (Mantella et al., 2008). Older adults could be at greater risk from age-related changes in neuroendocrine functioning and higher cortisol levels where mental health is concerned. This is because of the relationship between on-going high levels of glucocorticoids and impaired glucocorticoid receptor functioning in the amygdala and prefrontal cortex, areas that are particularly rich in glucocorticoid receptors and are associated with mood and anxiety disorder regulation (Glucocorticoid Cascade Hypothesis; Sapolsky, Krey & McEwen, 1986). This impaired functioning in these brain regions might then explain the association between higher cortisol levels and GAD in older adults (Mantella et al., 2008). This is in line with research more generally that has found that cortisol concentration levels increase with age (Stalder, et al., 2017) and with evidence of hypercortisolism in older adults (Gaffey, Bergeman, Clark, & Wirth, 2016).

Gender differences may also explain the inconsistencies in the literature. Higher morning cortisol concentrations combined with higher self-reported

depressive symptoms in adolescent boys indicate a greater risk of clinical major depressive disorder. In females, however, only the higher depressive symptoms represent a greater vulnerability (Owens, et al. 2014). Gender differences also indicate that under stressful situations, depression in men is associated with higher cortisol levels and this is moderated by anxiety (Zorn et al., 2017). In contrast, when women experience stress, depression results in a lower and flatter diurnal cortisol pattern whereas anxiety leads to higher cortisol levels (Powers, Laurent, Gunlicks-Stoessel, Balaban & Bent, 2016). A recent meta-analysis found gender differences even when there were no psychological disorders present, with men showing a 21% higher hair cortisol concentration than women (Stalder et al, 2017). Therefore it is important for research to differentiate between different participant groups and, specifically, to analyse for difference between the two gender groups to determine the degree of heterogeneity before further analysis is undertaken.

5.3.2 **Cortisol and Other Psychological Variables**

A heightened CAR has also been linked to other psychological variables besides depression and anxiety, raising the question of whether its association with pain might be through the behavioural and psychological response to pain rather than to on-going levels of pain (Sudhaus et al., 2012). The relationship, for example, might be moderated by more general levels of distress and negative emotions such as loneliness and sadness (Doane et al., 2013). Whilst a link between anxiety without comorbid depression and cortisol levels has not always been found, recent chronic life stress, negative emotion and general distress on the days on or immediately preceding cortisol testing have been associated with a flattened diurnal cortisol pattern and this has been the case amongst people without a diagnosis of psychopathology, as well as those with comorbid anxiety and MDD (Doane et al., 2013). Positive correlations have been found between salivary cortisol and helplessness (an element of catastrophic thinking) and between salivary cortisol and fear-avoidance, of which a key characteristic is pain catastrophizing, and this is also associated with distress (Sudhaus et al., 2012). Catastrophic thinking has been positively linked to elevated diurnal cortisol concentration levels,

resulting in a flattened morning cortisol pattern (Quartana et al., 2010), and with a higher CAR (Walton, MacDermid, Russell, Koren & Va Uum, 2013). This association has not always been found, however. Whilst greater pain was associated with a higher cortisol level across morning and afternoon time-points, this relationship was not found to be mediated by catastrophizing or by negative affect (Carlesso, Sturgeon, & Zautra, 2016). Some of the evidence indicates that catastrophizing could be an important mediator between hypercortisolism and pain, but as with other psychological variables, the relationship is not clear. Further research is needed to explore the role of catastrophic thinking and its association with HPA axis activity.

Pain acceptance refers to engaging in normal activities in spite of pain and ceasing trying to control or solve the problem of pain. There have been very few studies looking at the relationship between pain acceptance and cortisol concentration. Given the evidence associating acceptance with improved pain outcomes (see Section 6.4.2 Pain and Acceptance) it might be expected that there would be an associated improvement in cortisol levels. A yoga programme for women with fibromyalgia did result in greater acceptance, possibly through engaging in the activity, and higher overall cortisol secretion reflecting an improved diurnal cortisol pattern (Curtis, Osadchuk & Katz, 2011), but whether acceptance contributed to the cortisol levels is unclear. However, more compelling evidence has been found when considering people's ability to disengage from unattainable goals, which could link to stopping trying to solve the problem of pain where acceptance is concerned. Continued pursuit of an unattainable goal has been linked to increased psychological distress (Eccleston and Crombez, 2007), and psychological distress has been associated with alterations in immune system functioning (Segerstrom & Miller, 2004). It is possible therefore that acceptance and cortisol could be associated in this way. This was supported in a series of three studies demonstrating that goal disengagement predicts fewer physical health problems and reduced hypocortisolism, indicated through a steeper decline in cortisol across the diurnal rhythm throughout the day (Wrosch, Miller, Scheier & Brun de Pontet, 2007). This suggests that pain acceptance in the form of goal disengagement could have a positive effect on HPA axis activity, and on cortisol secretion

more specifically.

Despite the inconsistencies in the literature, the overall picture indicates that it is important to include a range of psychological variables, beyond simply anxiety and depression in isolation, when considering how they interact with the physiological functioning of the HPA axis and cortisol secretion. Given the established link between pain and psychological disorders (see Section 6.4.4), and the elevated risk of this for people with SCI, (see Section 6.4.4), if pain management programmes are to be effective, the relationship between psychopathology, psychological factors, cortisol and pain needs to be more clearly understood.

5.3.3 **Cortisol and Social Factors**

Positive social relationships are strongly associated with better health, so much so that people with good social relationships have a 50% increase in likelihood of survival (Holt-Lunstad, Smith & Layton, 2010). As previously highlighted, a flatter cortisol diurnal pattern has been linked to poorer health (Hackett, Steptoe & Kumari, 2014) and poor social relationships are associated with a flatter cortisol pattern (Slatcher & Robels, 2012), providing one explanation for the relationship between social support and health. So strong is the link between social support and health that a meta-analysis found that its effects on longevity were greater than more expected factors such as smoking, alcohol consumption and physical activity (Holt-Lunstad, Smith & Layton, 2010). This might be because as well as its positive effects on the HPA axis, it has additionally been found to attenuate activation of the autonomic nervous system (Uno, Uchino, & Smith, 2002; Roberts, Klatzkin, & Mechlin, 2015). Reductions in heart rate and blood pressure, for example, have resulted from positive social support and this has particularly been the case in stressful situations (Karlin, Brondolo, & Schwartz, 2003; Steptoe, 2000) and when experiencing pain (Che, Cash, Fitzgerald & Fitzgibbon, 2017; Roberts, Klatzkin, & Mechlin, 2015). In contrast, in female older adults, a greater risk of increased hypertension resulted from negative social interactions (Sneed & Cohen, 2014) suggesting that whilst positive social

engagement has healthful benefits, negative social exchanges do the opposite. The positive and negative effects of social support on health might, therefore, be mediated through various physiological systems, particularly the HPA axis and the autonomic nervous system (Ditzen & Heinrichs, 2014).

It has been suggested that there are two ways in which social support might impact the physiological stress response (Cohen & Wills, 1985). Firstly, the way a potential stressor is appraised might be moderated by social support in so far as with support from another individual the perception of threat might be reduced. The amygdala is the key structure that responds to threatening stimuli (Davis & Whalen, 2001) and it triggers activity in the HPA axis resulting in the release of cortisol. If a potential stressor is perceived as less threatening, activation of the amygdala will be reduced resulting in attenuation of the physiological stress response (Eisenberger, Taylor, Gable, Hilmert & Lieberman, 2007). The second way social support might impact the stress response is through enabling more successful coping or better emotion regulation (Cohen & Wills, 1985). Two brain structures are likely to be involved here. The ventrolateral prefrontal cortex (VLPFC) regulates distress caused by negative affect and pain (Hariri, Bookheimer, & Mazziotta, 2000; Ochsner et al., 2004), and the ventromedial prefrontal cortex (VMPFC) is involved in regulating or suppressing distress (Phan et al., 2005; Urry et al., 2006). When a threatening stimulus or stressor is perceived these structures might modulate amygdala activity, in turn impacting on HPA activity (Gold, Morey, & McCarthy, 2015). Other structures that have been implicated in social support and cortisol reactivity also show increased activation during distress caused by social separation: the dorsal anterior cingulate cortex (dACC), the frontal part of the cingulate cortex, and Brodmann's area 8 (BA 8), located in the frontal cortex. During a social rejection task, individuals who had strong daily social support had lower activation in these areas and this in turn was associated with reduced HPA activity (Eisenberger et al., 2007). This suggests that the dACC and the BA 8 could be important mediators between social support and cortisol reactivity.

Much research has found a link between lower psychological stress and close

social relationships or social support (Cohen, 2004; Karb, Elliott, Down & Morenoff, 2012). Participants who carried out a stress-inducing task without social support experienced higher anxiety, anger and negative affect than those who did receive social support (McQuaid et al., 2016). Given that acute states of these emotional responses usually elicit increases in HPA activity, it seems likely that stress might be buffered by the support of other people, resulting in attenuated cortisol secretion. A study examining attachment style and social support concurs with this. When combined with secure attachment style social support reduced psychological stress, and it decreased the cortisol response to stress when secure attachment style was controlled for (Ditzen et al., 2008).

This supports earlier work whereby men showed attenuated cortisol levels during a stress inducing activity when social support was provided by a female spouse (Kirschbaum, Klauer, Filipp, & Hellhammer, 1995) and also by a close friend (Heinrichs, Baumgartner, Kirschbaum & Ehlert, 2003). Results from a more recent female study also demonstrated that in stressful situations social support reduced salivary cortisol concentrations (McQuaid et al., 2016). However, it might be that social evaluation more specifically is the important social factor. In a performance situation, negative social evaluation, rather than just the presence of another person, has been linked to increased cortisol reactivity (Dickerson, Mycek & Zaldivar, 2008). In contrast, however, in response to an experimentally induced stressful situation, although daily social support provided at a high level predicted faster cortisol recovery when individuals were faced with a non-supportive audience, whether an audience were supportive or not did not affect cortisol levels differently (Taylor, Seeman, Eisengerger, Kozanian, Moore & Moons, 2010). Both situations increased the cortisol response suggesting that the anticipation of social evaluation might be sufficient to impact HPA activity, regardless of whether the attention is supportive or not (Taylor et al., 2010).

In support of this, both a higher CAR specifically and increased HPA axis activation more generally have been associated with social evaluative threat, a key component of social anxiety disorder (Dickerson & Kemeny, 2004) and the

HPA axis has shown high social sensitivity (Adam et al., 2014). The CAR is a strong predictor of first onset social anxiety disorder, but this has not always been found for other types of anxiety disorder (Adam et al., 2014), and in a recent study there was no relationship between anxiety and the diurnal rhythm more generally (Adam et al., 2014). Loneliness and social exclusion, both of which have been associated with social anxiety disorder (La Greca & Harrison, 2005) also predict higher CAR (Doane & Adam, 2010) and it is possible that this elevated CAR in turn increases the risk of anxiety disorders, especially those related to social interactions (Adam et al., 2014).

One aspect of social relationships that has received attention recently is that of partner responsiveness (Slatcher & Schoebi, 2017). Partner responsiveness relates to the extent to which an individual feels understood and cared for by their partner or by a significant person in their life (Slatcher, Selcuk & Ong, 2015). When combined with social support, this has been found to predict longevity (Selcuk & Ong, 2013) and as such might be another important factor in the association between relationships and health. In married couples, partner responsiveness has been found to predict psychological wellbeing, positive affect and negative affect (Selcuk, Gunaydin, Ong, & Almeida, 2016). In turn, flatter cortisol diurnal rhythm has been linked to negative affect (Polk, Cohen, Doyle, Skoner, & Kirschbaum, 2005), suggesting that partner responsiveness could have important physiological consequences. The link between perceived partner responsiveness and cortisol diurnal patterns has been identified longitudinally where over a 10-year period, responsiveness predicted a higher waking cortisol response and steeper cortisol slope. This was mediated in part by emotional support from the spouse and by a decrease in negative affect of the individual, but not associated with whether the relationship lasted over the 10-years or not (Slatcher, et al., 2015). This suggests that the impact of social relationships on HPA axis functioning may occur over a longer period of time but that also early social experiences can have long lasting effects on cortisol secretion. The implication of negative affect is of interest because of its possible mediating role between partner responsiveness and HPA activity. In this study a decline in negative affect between the two time points was associated with a more pronounced diurnal

cortisol rhythm and mediated the effect of higher responsiveness on cortisol slope (Slatcher et al., 2015). This implies that the psychological state of the individual combines with the way a partner responds to them to affect cortisol reactivity.

As summarised above, there is a body of research supporting the notion that social relationships impact on HPA activity and the resulting cortisol secretion. Added to this, it is possible that this relationship might be mediated by psychological factors such as negative affect, and that partner responsiveness is one aspect of the social relationship that might play an important role (Slatcher et al., 2015). It is therefore, important to analyse how these variables might interact to affect pain outcomes.

5.3.4 **Cortisol and Spinal Cord Injury**

Where SCI is concerned, cortisol and the HPA-axis might be important because of its neuroprotective effects, reducing inflammation and aiding repair following traumatic injury by inhibiting microglial cell activity (Gezici, Karakas, Ergün, & Gündüz, 2009). In the acute stages following SCI, microglial cells can worsen injury to the central nervous system by releasing pro-inflammatory cytokines (Kawabori & Yenari, 2015). This is known to be a particular problem in SCI where constant low-grade inflammation is apparent (Allison & Ditor, 2015) and where the injury compromises the effectiveness of the stress response (Kalpakjian, Farrell, Albright, Chiodo, & Young, 2009). Moreover, microglia and pro-inflammatory cytokines have been strongly associated with the onset of neuropathic pain (Milligan & Watkins, 2009), which is far more prevalent in the SCI population than in the general population (Siddall, McClelland, Rutkowski, & Cousins, 2003). Glucocorticoids such as cortisol act on cytokines in two ways: they suppress the pro-inflammatory cytokines and increase anti-inflammatory cytokines (Webster, Tonelli & Sternberg, 2002). However, as stated earlier, and demonstrated in Figure 11 below, on-going hypercortisolism can itself result in muscle and bone damage (McEwen, 2002) and suppression of the immune system (Nicolaides et al., 2015). Reduced immunity in turn leads to an increased risk of infection and slower wound

healing, which is known to be problematic for people with SCI (Allison & Ditor, 2015). For example, the greatest risk of morbidity and the most common reason for re-hospitalisation is pressure sores (Cardenas, Hoffman, Kirschblum & McKinley, 2004). In contrast, hypocortisolism can increase inflammation, which is already a problem in SCI, because the reduction in glucocorticoids results in a failure to suppress the pro-inflammatory cytokines (Webster et al., 2002). As highlighted earlier, where cortisol secretion and HPA activity are concerned homeostasis is vitally important, and this is particularly the case where SCI is concerned.

SCI shows the same pattern of acute and chronic effects with regard to HPA axis activity as psychological stress and anxiety conditions. People with acute SCI have shown increased cortisol levels and this has remained for three months following injury (Campagnolo, Bartlett, Chatterton, & Kellor, 1999). More recently, this was found to be the case in a study of Indian patients with cervical SCI, where evening and nighttime cortisol was higher than a control group, but there was not a significant difference in daytime levels. Overall, the mean levels of cortisol during the 24-hours were higher suggesting that patients with a recent SCI experience a disruption in the form of up-regulation to the cortisol diurnal rhythm (Fatima et al., 2016). In the longer term, chronic SCI cases show a blunted cortisol response and lower basal cortisol level associated with stress (Huang, Wang, Lee, & Lai, 1998; Kalpakjian et al., 2009). In this way both hypercortisolism and hypocortisolism can lead to a dysfunction of the immune system, with potentially serious consequences for people with SCI (Allison & Ditor, 2015).

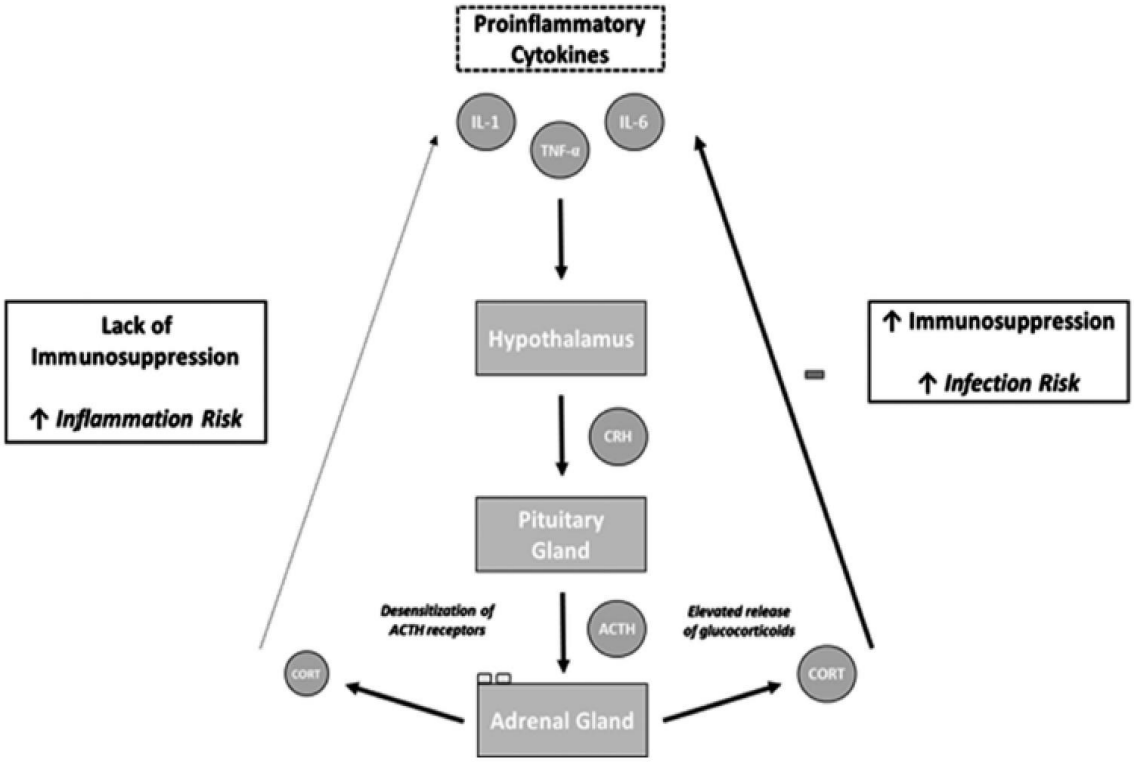

Figure 11. The HPA axis and inflammation. IL-1 = Interleuken 1; IL-6 = Interleuken 6; TNF-α = Tumor necrosis factor alpha (pro-inflammatory cytokine); CRH = Corticotropin-releasing hormone; ACTH = Adrenocorticotropic hormone; CORT = Cortisol. Proinflammatory cytokines have the capability of upregulating the HPA axis. This stimulates a cascade whereby corticotropin releasing hormone (CRH) induces the pituitary gland to release ACTH, which then induces the release of glucocorticoids such as cortisol (CORT) from the adrenal gland. Glucocorticoids induce immunosuppressive effects. Therefore, under conditions of chronically elevated proinflammatory cytokines, elevated levels of circulating glucocorticoids and a corresponding immunosuppression may result. Alternatively, prolonged overactivation of the HPA axis may result in a desensitization of ACTH receptors on the adrenal gland resulting in a reduction in glucocorticoid release and a lack of immunosuppression, allowing for elevated levels of proinflammatory mediators. From "Immune Dysfunction and Chronic Inflammation Following Spinal Cord Injury," by D. J. Allison and D. S. Dittor, 2015, *Spinal Cord, 53*, p. 16. Copyright 2015 by Springer Nature Publishing AG.

In addition to the potential negative biological effects of stress for people with SCI, it can also have poor psychological consequences. Perceived stress has been associated with increased depression and anxiety, and reduced quality of life and social support in veterans with SCI (Rintala, Robinson-Whelan & Matamoros, 2005). This study also found that when people did not have good

perceived social support, the negative consequences of stress were more severe (Rintala, Robinson-Whelan & Matamoros, 2005). Therefore, both the physiological and the psychological consequences of stress can be particularly problematic for people with a SCI.

5.4 Conclusion

In conclusion, it has been demonstrated that stress and distress, and the resulting physiological response, are major factors in many health disorders, including chronic pain. The literature in the able bodied population is mixed with regards to the nature of the association between cortisol and depression, anxiety and catastrophic thinking. Very little research has looked at the association between cortisol and other psychological factors. There is clearer evidence that social support affects HPA axis activity. However, in the SCI population cortisol has only been explored in relation to the injury, rather than in relation to pain, and its association with other psychosocial variables has not been the focus at all. Additionally, the majority of research has been carried out in the United States of America (USA) and Canada. Whilst there has been some interest in this area across Europe, very few of these studies have involved The United Kingdom (UK). It is therefore essential to understand how the stress system interacts with other psychological and social factors in a UK based SCI population, in order to develop effective stress management and pain management strategies. This could lead to an improvement in health in general and to pain outcomes specifically (Nicolaides et al., 2015).

6 Chapter 4 - Psychological Theories of Pain

In accordance with the biological theories of pain, psychological theories have also emphasised the role of both bottom-up and top-down processes in the experience of pain. However, where the latter are concerned, the moderation or amplification of pain comes from psychological factors. It has been widely reported that the relationship between pain and distress is influenced to a large extent by cognitive and behavioural elements (Turk, Swanson, & Tunks, 2008). In the spinal cord injured population psychological problems were the most frequently cited difficulties associated with both acute and chronic pain (Tran, Dorstyn & Burke, 2016), and pain, over a six-year period, is the greatest predictor of poor social integration and psychological functioning (Jensen, Moore, Bockow, Ehde, & Engel, 2011). This reinforces the need to adopt a biopsychosocial approach to understanding pain in SCI and in implementing appropriate treatment options in the context of that model. The following sections discuss three different theoretical perspectives regarding pain and psychology, and then reviews the literature on the specific psychological factors pertinent to this thesis: pain catastrophizing, pain acceptance, mental defeat and anxiety and depression. It is noted that these factors, when they are present, do not exist independently of one another, but that they become an integrated part of the pain experience. However, they have been discussed individually in this thesis for the purposes of clear presentation.

6.1 The Cognitive-Affective Model and the Neurocognitive Model of Attention to Pain

The Cognitive-Affective model considers attention to be a key factor in the experience of pain and demonstrates pains interruptive function (Eccleston and Crombez, 1999). Three aspects of the relationship between attention and pain are highlighted. Firstly, paying attention to the pain means that goal-directed actions can be taken to escape it. Secondly, these actions to escape pain take precedence over other tasks and thus disrupt attention and behaviour from other activities. Thirdly, the interruption caused by pain is moderated by aspects of the pain itself and by aspects of the pain

environment, for example, emotional arousal (Eccleston & Crombez, 1999). Factors relating to pain include the intensity of pain with high intensity being more disruptive than low intensity in patients experiencing chronic pain (Eccleston, 1995b). Other studies suggest that novelty (Legrain et al., 2009) and the threat of pain increase its salience, which in turn makes it more likely to be selected for attention (Crombez et al., 1997; Crombez et al., 1998a). Pain is also more likely to interrupt attention in those who catastrophize about the pain (Crombez et al., 1998b) and in those who have a high awareness of somatic information (Eccleston et al., 1997). Where the latter is concerned, the heightened vigilance that goes with this ensures that pain is quickly selected above competing demands (Eccleston et al., 1997).

Where the environment of pain is concerned, most research has focused on the efficacy of distraction tasks at reducing either the pain threshold or its disruptive capacity. The evidence is inconclusive regarding the complexity or difficulty of distraction tasks. It is possible that distraction tasks might be more efficacious when pain intensity is low and distraction tasks difficult (McCaul and Malott, 1984). However, Hodes, Howland, Lightfoot, and Cleeland (1990) found no difference between high and low distraction conditions where pain tolerance and pain ratings were concerned. There has been more consistent support where the emotional significance of the task is concerned. Thinking about something pleasant can increase tolerance to pain when compared to thoughts about unpleasant or anger inducing situations (Stevens, Heise and Pfost, 1989). It has been suggested that two possible processes might be involved here. It might be that the affective response matches the emotional state of the individual and so is facilitated, whereas those that do not match are inhibited. This supports the attentional set hypothesis, that states that individuals display bias towards only attending to the sensory stimuli that are relevant to the task in hand, ignoring other stimuli (Legrain et al., 2009). Another possibility is that emotions are as demanding of attention as pain, so attention is re-focused away from pain. This suggests that affective-motivational aspects of the environment of pain might be significant moderators of its interruptive ability (Eccleston and Crombez, 1999). Verhoeven et al. (2010) support the significance of motivation. They found that

for high catastrophisers the effects of distraction tasks were increased if they were of motivational relevance to the individual. However, distraction may not always be effective. Individuals with a lower pain threshold and who demonstrate an attentional bias towards pain cues benefit less from distraction tasks (Van Ryckegham, Crombez, Van Hulle and Van Damme, 2012).

This model takes account of the various factors that moderate the interruptive function of pain (Eccleston and Crombez, 1999). The model argues that the environment provides multiple demands on attention. The stimuli that are attended to pass through the sensory system. One of these is selected as the focal task and initiates action, for example, if hunger is selected as the focal task the action is likely to be concerned with eating to reduce the hunger. The model also recognises that there are moderators that operate between the sensory system and the action programmes, ensuring an efficient and coherent selection of stimuli and action decisions. If a stimulus is threatening, like for example pain, this interrupts the focal task and attention is switched to the painful stimulus and actions are initiated to deal with it. When pain is relieved or reduced, attention is switched back to the focal task. Where chronic pain is concerned switching occurs repeatedly between the chronic pain and other demands as a way of coping (Eccleston & Crombez, 1999).

The Neurocognitive Model of Attention to Pain (Legrain et al., 2009) further develops the role of attention in the pain experience by suggesting that both bottom-up and top-down processes are utilised in attentional selection. Bottom-up processes ensure that salient and novel stimuli are attended to, of which pain would be a good example, and that appropriate action is then taken. Neuroimaging studies have provided support for this by demonstrating increased activity in the midcingulate cortex in response to pain (Downar, Mikulis, & Davis, 2003). This area is associated with novelty detection (Downar, Crawley, Mikulis & Davis, 2002) and control of behaviour (Botvinick, Cohen & Carter, 2004). Top-down processes are goal-directed in that they analyse the current situation or task, and prioritise incoming information according to its relevance. It is thought this occurs through inhibiting neuronal activity to irrelevant stimuli whilst increasing the response of neurons to

relevant stimuli (Desimone & Duncan, 1995). In relation to chronic pain, paying attention to pain is likely to lead to hypervigilance, with pain demanding on-going and increasing attention (Crombez, Van Damme & Eccleston, 2005).

Studies supporting the neurocognitive and the cognitive affective models and the role of attention in the pain experience have demonstrated that the presence of pain can reduce task performance (Eccleston, 1995), whereas engaging in a cognitively demanding task reduces the threat of pain and catastrophic thinking (Sullivan, Bishop, & Pivik, 1995). This suggests that a demanding task takes a high level of cognitive investment, which could subsequently lead to reduced pain because less attentional resources are allocated to it. However, although these models provide a convincing argument for the way in which attention is interrupted by pain, they assume that the experience of pain is mainly a bottom-up process and it does not account for chronic pain, which may not have a pathological cause. They also focus on the role of attention, and in doing so place less emphasis on the role of the social environment, behavioural factors and psychological variables that are known to be involved.

6.2 The Fear-Avoidance Model of Pain

The Fear-Avoidance Model (Vlaeyen & Linton, 2000) goes some way towards meeting the deficits of the cognitive affective and neuro-cognitive models by acknowledging the mediating role of psychological factors in the pain experience. Figure 12 provides a graphical interpretation of the model. It describes how when injury leads to a pain experience, pain catastrophising, made worse by negative mood and threatening illness information, increases fear and avoidance behaviours leading to disuse, depression and disability. This becomes a negative cycle. However, if the pain does not instigate a fear response, the individual is more likely to confront it and achieve recovery.

Permission for inclusion not obtained

Figure 12. The `fear'-avoidance model depicting how, following injury, an individual's pain experience either leads them to catastrophize, resulting in fear, avoidance and hypervigilance, disability and on-going pain, or to confront and recover from the pain. See text for full description. Adapted from "Fear-avoidance and its consequences in chronic musculoskeletal pain: a state of the art," by J. W. S. Vlaeyen and S. J. Linton, 2000, *Pain, 85*, p. 329. Copyright 2000 by the International Association for the Study of Pain.

The model explains how the extent of protective behaviours adopted in response to pain, such as withdrawing from the painful stimulus, might be better predicted by the meaning of the pain to the individual rather than by the pain itself (Arntz & Claassens, 2004). It is also suggested that whilst this protective responding may be adaptive in nature in the short-term, it may worsen the problem in the long-term (Crombez, Eccleston, Van Damme, Vlaeyen, & Karoly, 2012). Pain is often perceived as threatening which leads to pain-related fear, which is important in the development of disability. The fear-avoidance model explains how one such protective behaviour, avoidance, leads to distress and pain disability. The avoidance is motivated by fear but it remains unclear how this pain-related fear occurs to start with (Vlaeyen & Linton, 2012).

In trying to answer this question, Vlaeyen and Linton (2012) considered the role of classical conditioning and suggested that pain is an unconditioned stimulus that sets off our defensive system. When an association is made between the pain and another stimulus, such as interoceptive stimuli (providing afferent information from the body) or proprioceptive stimuli (concerning movement and posture) the conditioned response becomes fear. Fear itself then triggers the defensive system. For example, Meulders, Vansteenwegen and Vlaeyen (2011) found that pairing an upward movement of a joystick with a painful shock to the hand increased fear of movement–related pain. The movement itself became the conditioned stimulus and was enough to activate the conditioned response of fear. This suggests that learning of this nature has an important role in how pain-related fear occurs. It has been proposed that there are three ways in which such learning is obtained (Vlaeyen and Linton, 2012). Firstly, people learn through direct

experience, as evidenced by Meulders et al. (2011). Secondly, people learn through verbal information, for example, being warned that a particular action may result in injury and pain (Vlaeyen, et al., 2009). Thirdly, people learn through observation, whereby seeing another in pain leads to a learnt fear of that pain stimulus. What is less clear is how these three pathways might interact with each other, for example, how previously observing someone in pain might enhance learning if that person then experienced a similar painful event. Also, it is unclear if one pathway to learning has a greater impact than the others (Vlaeyen & Linton, 2012).

It is possible that there are differences between unpredictable and predictable pain (Vlaeyen and Linton, 2012). Unpredictable pain may cause more distress than pain that can be predicted because it might produce a more general form of distress involving worry and apprehension that can impact on the intensity of the pain experienced (Vlaeyen and Linton, 2012). This idea was supported by Meulders et al. (2011) who found that the unpleasantness of pain and pain intensity were both rated higher when pain was unpredicted. However, further research is needed to assess the effects of different aspects of unpredictability such as the duration of pain, its intensity and its location. It may be that one aspect is more important than others in the experience of pain and pain-related fear, rather than simply being to do with general unpredictability.

Whilst there is much evidence to support the fear-avoidance (FA) model, Crombez, et al. (2012) have identified three challenges to it. Firstly, they point to and question the validity of its psychopathological roots. They suggest that the unhelpful beliefs held by people with chronic pain, for example that pain equals harm, rather than being irrational, are in fact culturally endorsed. In psychopathology and in the FA model, according to the authors, pain is seen as being a normal situation and it is the patients response which is considered abnormal. However, in chronic pain it is more likely that the pain is abnormal and the way in which patients respond is culturally defined, generally from a biomedical framework, and is normative (Crombez et al., 2012). Also, they suggest that the role of pain intensity has been understated in the FA model.

The second challenge concerns the failure of the FA model to consider the dynamics of functional recovery, or how patients attempt to recover and how they try to function despite the pain and disability. It focuses more on pain as a sign of bodily harm, whereas it can also be something that obstructs participation in valued activities and interferes in the individuals daily life (Karsdorp & Vlaeyen, 2011). The degree of life interference caused by pain-related disability is a better predictor of how frequently individuals seek support from healthcare providers than the pain itself (Ferreira et al., 2010). Additionally, the focus of the model is on the vicious cycle of fear and avoidance leading to increased disability rather than explaining the way in which confronting pain might be adaptive and lead to recovery (Crombez et al., 2012).

The third challenge is that the FA model has ignored the motivational context of competing, multiple goals. Crombez et al. (2012) suggested that pain and avoidance should be considered in the light of other goals, whereby goal facilitation, when the pursuit of one goal helps to achieve another, and goal interference, when the pursuit of a goal interferes with achieving another, may play a part in pain-related fear. It might not simply be about avoidance behaviour being motivated just by fear. In certain situations another goal may have such value that the individual doesn't avoid but confronts the pain. The FA model assumes that these two behaviours, confronting and avoiding, are stable. A motivational perspective suggests that depending on the situation and value of the goal, a confronter could become an avoider and vice versa (Vlaeyen & Morley, 2009).

The central idea here is that pain is not just associated with harm but rather it disrupts the individual's pursuit of daily goals, which has a negative effect. The motivational perspective is built around the idea of self-regulation (Van Damme, Crombez, & Eccleston, 2008). If a goal is unattainable then the individual needs to be able to disengage from it and re-engage with an alternative goal. When people are able to do this it improves quality of life and reduces the negative effects of goal failure, with individuals reporting higher ratings of subjective well-being (Wrosch, Scheier, Miller, Schultz and Carver,

2003). As suggested by the neurocognitive model (Legrain et al., 2009), when in pursuit of goals, people tend to pay greater attention to goal-relevant information than irrelevant information. This may mean that when people are pursuing a valued goal they might be less sensitive to pain (Van Damme, Legrain, Vogt, & Crombez, 2010) and if the goal has higher value to the individual they will be more persistent in their pursuit of it (Crombez et al. 2012).

6.3 The Misdirected Problem Solving Model of Pain

In order to take account of motivational and goal-directed behaviours, Crombez et al (2012) suggested that the fear-avoidance model should be redefined in the context of the Misdirected Problem Solving Model (Figure 13; MPM; Eccleston & Crombez, 2007). Fear-avoidance behaviours occur when pain interferes with the achievement of valued goals, and persistent attempts to restore these goals fail. In this context, rigid problem solving attempts result from the idea that in order to resume daily life pain must be reduced.

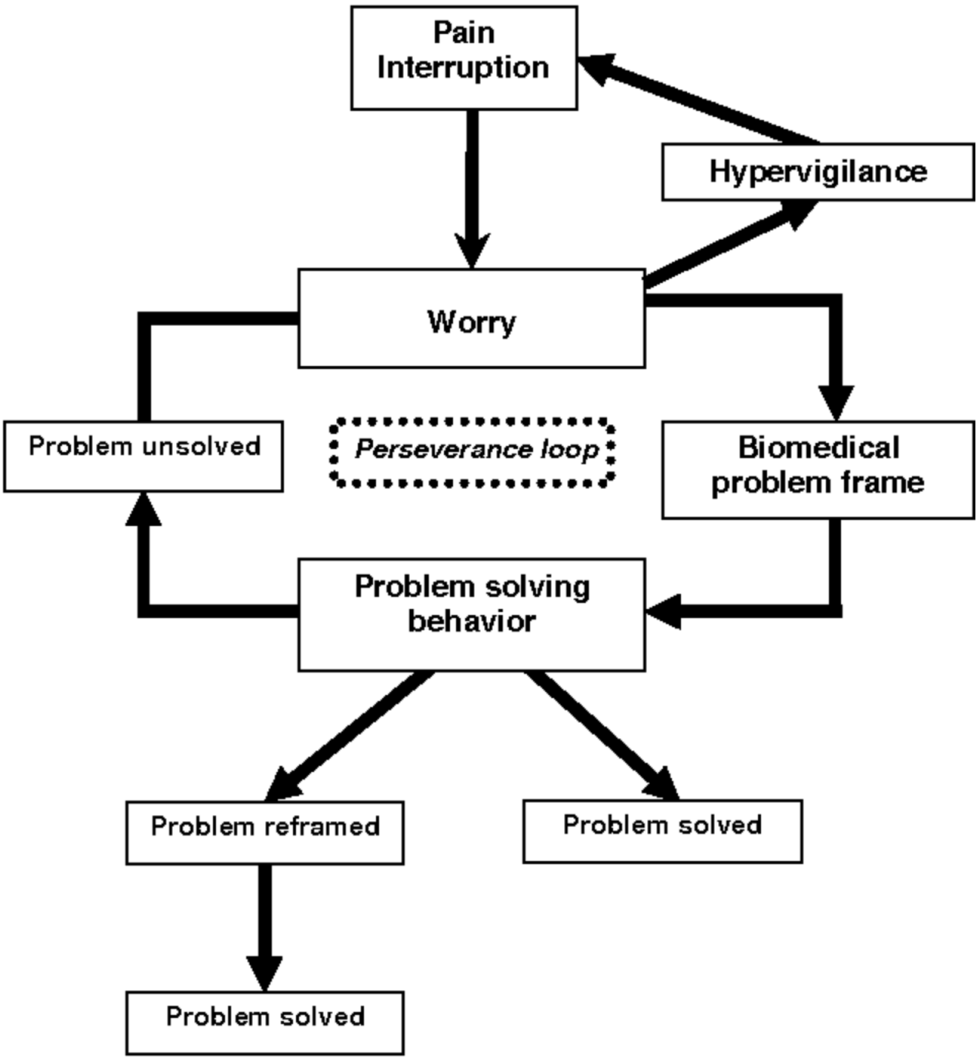

Figure 13 The Misdirected Problem Solving Model. Graphical depiction demonstrating how worry leads to hypervigilance and problem solving, which can result in the problem being solved, but if unsuccessful can lead to the individual becoming stuck in the perseverance loop. Adapted from "Worry and chronic pain: A misdirected problem solving model" by C. Eccleston and G. Crombez, 2007, Pain, 132, p. 235. Copyright 2007 by the International Association for the Study of Pain.

The misdirected problem-solving model (Eccleston & Crombez, 2007) builds on the FA model and demonstrates how the focus on problem solving, driven by worry, can become problematic. It identifies that when pain interrupts attention, causing worry and hypervigilance it is often framed as a biomedical problem. Problem solving then focuses on reducing or removing pain. If this is successful the pain will reduce and so will the worry. However, with chronic

pain, this strategy is often unsuccessful which increases worry. The individual then perseveres with trying to solve the problem and becomes stuck in what the authors term a perseverance loop. The patient continues to look for a solution, even though their own experience suggests there is none. The problem frame is narrowed and the worry and distress are maintained.

The model proposes that sometimes problem solving can be detrimental to the wellbeing of individuals with chronic pain, with worry related to the perceived threat of danger (the pain) being the driver for problem solving (Eccleston and Crombez, 2007). The worry is problematic because it serves to maintain vigilance to the pain and keeps the focus on solving the problem of it. Patients with chronic pain report their worry about pain as being attentionally demanding, harder to control and more distressing than worry about other things. They also report worrying for longer about pain (Eccleston, Crombez and Aldrich, 2001). It is likely that such experiences of worry would lead to repeated attempts to solve the problem of pain in order to reduce the worry.

When patients are stuck in the perseverance loop they may be more rigid in the way they think about pain and less likely to take account of information that suggests they are framing the problem incorrectly (Eccleston and Crombez, 2007). Any attempts by others to change the problem frame are likely to be viewed as a rejection (Eccleston, Williams, Stainton Rogers, 1997). The perseverance loop might, therefore, explain why chronic pain patients have a high demand for medical services as they continue to seek to remove the pain they experience (Eccleston & Crombez, 2007). Ultimately, the continuing worry can have a negative impact on health, increasing disability.

These psychological models and theories have helped to move the understanding of pain further away from a purely biomedical approach, and firmly established the presence of psychological features in the experience of pain. A more detailed analysis of how these features impact the pain experience, both in the able bodied population and for people with SCI, can be found below.

6.4 Psychological factors associated with pain

6.4.1 Pain Catastrophizing

Pain catastrophizing has been defined as “an exaggerated negative mental set brought to bear during actual or anticipated painful experiences” (Sullivan et al., 2001, p.53). As this definition suggests, people who score highly on pain catastrophizing measures tend to exaggerate their experience of pain, thinking of it as the worst pain they have ever had and that it will never end. Catastrophic thinkers also anticipate future pain episodes in a similarly negative way. It has been suggested that catastrophizing has three dimensions; magnification where the perception of pain is exaggerated, rumination where attention is directed to the pain and helplessness where the individual believes that there is nothing they can do about the pain (Sullivan, Bishop & Pivik,1995). The validity of these dimensions has since been supported by psychometric investigations (Osman et al., 1997; Van Damme, Crombez, Bijttebier, Goubert, & Van Houdenhove 2002).

Catastrophizing is an important factor to consider where pain is concerned because high levels of catastrophic thinking have been causally linked to pain (Sullivan et al., 1995, Sewell, et al., 2018), to pain and illness behaviours (Sullivan et al., 2000), to decreased quality of life (Sewell et al., 2018) and to disability (Sullivan et al. 1998). It has also been associated with the development from acute to chronic pain (Edwards, Dworkin, Sullivan, Turk and Wasan, 2016) and is a strong predictor of persistent pain (Lewis, Rice, McNair & Kluger, 2015).

Longitudinal studies provide support for the role that catastrophizing plays in the maintenance of chronic pain, for example, pain catastrophizing precedes increases in pain responses (Campbell et al. 2010), and has been associated with increased pain and a reduction in the benefits of pain treatments (Vissers et al., 2012). The negative effect that catastrophizing has on pain treatments

has been found in both analgesic medication (Schiphorst Preuper et al., 2014) and in psychological treatment (Smeets, Vlaeyen, Kester, & Knottnerus, 2006). Therefore, as well as having a negative effect on an individuals pain experience, pain catastrophizing also hampers efforts to treat pain. Because of its impact, pain catastrophizing is an important construct to consider in implementing efforts to manage pain and when supporting people who are experiencing pain. However, it has been suggested that pain catastrophizing reflects the same underlying construct as depression and anxiety, given that positive correlations have been found between these factors (Sullivan et al., 1995). It is important to consider, however, that when depression and anxiety have been controlled for catastrophizing is still associated with disability and is able to predict pain (Sullivan et al., 1998; Sullivan et al., 1995). This indicates that it is more likely to be a separate construct, and therefore, one that needs to be considered separately to these other psychological factors.

Several theoretical models have been proposed that could provide a framework for better understanding catastrophizing; a schema-activation model (Beck, 1979), a communal coping model (CCM; Sullivan et al. 2001), an appraisal model (Severeijns, Vlaeyen and van den Hout, 2004), and an attentional model (Quartana, Campbell, & Edwards, 2009). The schema-activation model (Beck, 1979) suggests that individuals possess pain schema that develop through learning processes and experience. These may contain negative information about pain leading to a greater focus on it and pessimistic beliefs about the high threat value of pain and the ability to cope with the experience of it. This could lead to increased pain and disability once those schemas are activated. What might activate the schemas is not clear but it is possible that hypervigilant body scanning could be involved in chronic pain conditions. Even a slight indication of discomfort would lead to greater attention being given to pain and this could be sufficient for schema activation. However, Sullivan et al. (2001) have found that catastrophizing scores taken during pain-free periods are still predictive of future pain. This suggests that pain may not be essential for schema activation to occur (Sullivan et al., 1995).

Pain catastrophizing may better be conceptualised as an attention or information processing bias. Here, an individual may pay an exaggerated amount of attention to pain and sensory information resulting in an amplification of the pain experience (Quartana et al., 2009). This idea is supported by Van Damme, Crombez and Eccleston (2004) who found that high catastrophizers were likely to assume that pain cues would always be followed by pain experiences and that these cues would result in the engagement of negative pain schemas. This suggests that people who score higher on pain catastrophizing measures pay more attention to their pain and find it harder to disengage from it. Where the attentional model is concerned, the magnification and rumination dimensions of catastrophizing are particularly important. When the threat of pain is exaggerated (magnification), and pain-related thoughts are not suppressed (rumination), attention will be focused towards the pain, increasing the intensity of it (Sullivan et al., 2001).

Catastrophic thinking then, increases attention towards threatening somatic information and rumination about the pain (e.g. Crombez, Eccleston, Baeyens & Eelen, 1998b; Eccleston & Crombez, 1999; Eccleston, Crombez, Aldrich & Stannard, 1997), therefore, attention may be a critical factor in the relationship between catastrophising and the experience of pain (Sullivan et al., 2001). The schema-activation model (Beck, 1979) and the attentional model (Quartana et al., 2009) both focus on catastrophizing as a cognitive process and it has not been thought of as a coping strategy in this literature (Sullivan et al. 2001). The CCM of catastrophizing (Sullivan, 2012), however, proposes that catastrophic thinking may serve as a coping mechanism if part of the goal of such a mechanism is to increase support or assistance. In order for such a goal to be achieved the distress of the individual must be communicated effectively to others in their social environment. This is achieved through the verbalisation of the catastrophic thinking. When others respond solicitously it serves to reinforce this type of pain behaviour.

The fact that spouses of higher catastrophizing patients rated them as less able to cope with pain (Keefe et al., 1997) supports the idea that catastrophizing has a communicative function. This has been further

demonstrated by the increased use of first person singular pronouns in reflective essays written by people experiencing pain, reflecting the association between high catastrophizing and a greater focus on the self (Junghaenal, Schneider and Broderick, 2017). Additionally, high catastrophizers also make more references to other people, supporting the idea that catastrophizing may be a tool used by individuals to include others in their pain experience and inform them about the pain and distress being experienced (Junghaenal et al., 2017). In this way, verbalising catastrophic thoughts communicates the distress being experienced and serves as a coping strategy by gaining support from others.

Support for the CCM has also been seen amongst people with SCI, whereby people living with a spouse or partner have a stronger association between catastrophizing and sensory pain than people living with someone else (Giardino, Jensen, Turner, Ehde and Cardenas, 2003). This might be because a spouse or partner provides a safe place in which to verbalise catastrophic thinking. Furthermore, a stronger association was found between catastrophizing and affective pain for people who received more solicitous responses to their pain behaviours. It is possible that the solicitous response serves to reinforce the catastrophizing behaviour and the negative pain appraisals that drive it (Giardino et al, 2003). If pain treatment is to be effective, consideration needs to be given to the interpersonal relationships that exist for an individual in pain and how the response to pain by a significant other person can exacerbate that pain, even when the response is solicitous rather than negative. This will be discussed further in Chapter 5.

Despite the support for the CCM, the theory fails to recognise the context of competing goals where pain catastrophizing is concerned (Caes, Goubert, Sullivan and Chambers, 2013). Whilst catastrophizing may have a communicative function and this might be concerned with getting support to better cope with the pain, along side this the individual may have additional goals concerned with pain reduction, social activities, or work commitments (Caes, et al., 2013). It can also be questioned whether the CCM provides an accurate or helpful conceptualisation of catastrophizing, as it can be argued

that catastrophic thinking has a cognitive connotation which is not recognised by the CCM (Severeijns, Vlaeyen, & van den Hout, 2004) and that a cognitive process such as catastrophizing should not be explained solely in terms of its function. Catastrophizing might, therefore, be better understood within the framework of an appraisal model (Severeijns et al, 2004).

The appraisal model suggests that catastrophic thinking causes individuals to focus their attention on pain because the pain is appraised as threatening. In support of this, high catastrophic thinking has been associated with strong fear-avoidance beliefs, which negatively affect quality of life and disability (Shim et al., 2018). The dimensions of magnification, rumination and helplessness map onto the transactional model of stress (Lazarus and Folkman, 1984). This suggests that when faced with a stressful situation, primary and secondary appraisals are carried out. The primary appraisal assesses how stressful the situation is and the secondary appraisal assesses how well the individual thinks they will be able to cope with it. Where catastrophizing is concerned, magnification and rumination form the primary appraisal by focusing attention on the pain and magnifying its threat. Helplessness takes the form of the secondary appraisal with the individual believing there is nothing they can do about the pain (Sullivan et al., 2001). This model focuses on the cognitive nature of catastrophizing and explains how the display of distress that such appraisals evoke are likely to attract attention and social support, rather than catastrophizing having this as a function. High catastrophizers, therefore, may be more likely to seek out social support because they feel helpless in coping with the pain and view the pain as more threatening (Severeijns et al, 2004). Evidence that catastrophizing is linked to cognitive appraisal processes has been found in a number of studies (e.g. Geisser, Robinson & Riley, 1999; Turner & Clancy, 1986) supporting the validity of this model as a theoretical framework for catastrophizing.

However, it has been argued that the current literature proposing these four models takes a narrow view of catastrophizing and fails to fully explain its function (Flink, Boersma, & Linton, 2013). Models such as the CCM (Sullivan et al., 2001) and the Misdirected Problem-Solving Model (MPM; See Section

6.3 for information about the MPM; Eccleston & Crombez, 2007) go some way towards identifying the function of catastrophizing but their explanations are both context dependent; the CCM places the function in a social context whereas in the MPM the context is one of problem solving. Catastrophizing might better be thought of as a form of repetitive negative thinking which has the function of regulating negative emotions by reducing the intensity of the fear response (Flink et al., 2013). It does this by avoiding the processing of emotional responses and can therefore be considered an avoidant coping strategy. This also suggests that catastrophizing has a problem-solving function; to solve the problem of pain initiated negative emotions.

However, Flink et al. (2013) suggest that whilst this idea of catastrophizing supports the central concepts in both the CCM and the MPM, it is not dependent on those narrow contexts and therefore, provides a broader conceptualisation of catastrophizing which they prefer to refer to as 'catastrophic worry'. This alternative term encapsulates the idea of catastrophizing as a process incorporating behaviour, thoughts and emotions and is supported in the anxiety literature (Davey & Levy, 1998) where catastrophic worriers are defined as having a "general perseverative iterative style", "couching their worries in a way that reflects personal inadequacies and insecurities", and that worriers believe their catastrophic thoughts contain relevant information (Davey & Levy, 1998, p. 583). The three parts of this definition map directly onto the three dimensions of catastrophizing; rumination, helplessness and magnification respectively, and as such does not move too far from the current view of catastrophizing and brings the concept within the field of pain in line with the concept in other areas (Flink et al., 2013). If catastrophizing can be understood as negative thinking then treatments such as Cognitive Behavioural Therapy could be efficacious and as such the reliance on medication could be reduced.

A further consideration is whether catastrophizing can be better thought of as a single construct or whether the dimensions of magnification, rumination and helplessness might contribute differently to pain-related outcomes. Some differences have been found previously, for example, in people with various

neuropathic pain conditions where a significant relationship between catastrophic thinking and neuropathic pain has been demonstrated, but only with the helplessness subscale (Sullivan, Lynch & Clark, 2005). As helplessness has also been found to be important in chronic nociceptive pain it might reflect the emergence of helplessness during long periods of suffering (Sullivan et al., 2005). In contrast to this, other research has found that magnification rather than helplessness uniquely predicts pain ratings (Sullivan, Stanish, Sullivan & Tripp 2002). However, both helplessness and magnification have been associated with various pain outcomes; specifically helplessness has uniquely explained the variance in the prediction of pain severity, supporting Sullivan et al. (2005) and both helplessness and magnification have predicted quality of life and depressed mood (Craner, Gilliam & Sperry, 2016).

Rumination has not always predicted any of the pain related outcome variables (Craner et al., 2016). An explanation for the differences between these dimensions might be that the particular dimension of catastrophic thinking may change with the chronicity of the pain. As the pain condition continues people's feelings of helplessness regarding their ability to cope might increase along with the tendency to magnify the awfulness of their experience (Craner et al., 2016). Research provides support for this idea. Magnification has been associated with pain one year after a whiplash injury (Lefebvre, Lester & Keefe, 1995), the best predictor of disability after three years of pain has been found to be rumination (Sullivan, Stanish, Waite, Sullivan and Tripp, 1998) and Vienneau, Clark, Lynch and Sullivan (1999) suggest that helplessness was a better predictor of disability in long-term pain. This indicates that rather than having a general focus to pain treatments regardless of chronicity, the focus of treatment where catastrophizing is concerned needs to be dependent on the length of time for which pain has been experienced. For more recent pain conditions, interventions to reduce magnification and rumination might be more effective whereas if pain has been experienced for many years helplessness might need to be the focus.

Where treatment is concerned it is also important to consider gender

differences in both the pain experience and in catastrophic thinking, for example, women have been found to score higher on measures of catastrophising than men (Sullivan, Tripp & Santor, 2000) although Sullivan et al. (2000) only found this to be the case on the rumination and helplessness subscales of the Pain Catastrophising Scale (Sullivan et al, 1995). Women also tend to display more pain behaviours and report higher levels of pain (Sullivan et al., 2000). Catastrophic thinking might account for this. When catastrophizing is controlled for there is no significance in the gender differences in pain intensity ratings and pain behaviour (Sullivan et al., 2000), indicating that women may adopt greater catastrophic thinking than men, leading to the increases in pain behaviours and pain intensity ratings.

More recently, it has been suggested that the way affective or sensory pain is combined might account for the gender-dependent effects on catastrophizing. Higher catastrophic thinking in men was associated with high sensory pain when affective pain was low or average, but not when it was high. In contrast, high catastrophic thinking in women was associated with high affective pain regardless of sensory pain (ChongNak, Daegu, Jeongwi, & Sungkun, 2019). This implies that men and women may respond differently to the affective and sensory characteristics of pain. Where gender and pain modulation is concerned, the literature has been inconsistent. Some studies have reported a lower diffuse noxious inhibitory control (DNIC) effect for women than for men (Ge, Madeleine & Arendt-Nielson, 2004; Serrao et al, 2004), whereas others have found no difference (e.g. Baad-Hansen, Poulsen, Jensen, & Svensson, 2005). DNIC refers to an inhibitory mechanism that modulates the experience of pain by weakening the activity of pain-signalling neurons in the dorsal horn of the spine. Weissman-Fogel, Sprecher and Pud (2008), in a regression analysis, found that gender did predict the effectiveness of DNIC but not once catastrophizing was controlled for. This suggests that the level of catastrophic thinking may be a better predictor of the effectiveness of DNIC than gender and that catastrophizing might mediate the relationship between gender and pain modulation (Weissman-Fogel et al., 2008). Further research is needed to determine the mediating role of catastrophic thinking.

The link between pain catastrophizing and changes in central nervous system mechanisms has been quite widely reported. The negative correlation found between pain catastrophizing and DNIC (Weissman-Fogel et al., 2008), implies that pain catastrophizing might impact the pain experience through pain modulation systems such as descending pain inhibitory pathways. This has been supported by Seminowicz and Davis (2006) who used functional magnetic resonance imaging (fMRI) to examine the neural correlates of pain catastrophizing. They found that during mild pain, catastrophizing had a positive association with activity in areas of the brain concerned with motor and affective aspects of pain and attention such as the parietal cortex, the insula and the dorsolateral pre-frontal cortex. The insula is thought to be associated with attention (Downar, Crawley, Mikulis & Davis, 2000) so this might reflect the activation, linked to pain catastrophizing, of a “pain vigilance signal” (Seminowicz & Davis, 2006, p. 301).

Seminowicz and Davis provide further support for this. They found that higher scores on pain catastrophizing measures were negatively correlated with lower pain thresholds, which might reflect heightened vigilance, and positively correlated with the use of a greater number of affective words to describe pain, indicative of an increased emotional response to pain. During more intense pain, catastrophizing was negatively correlated with activity in parts of the prefrontal cortex that are involved in the descending modulation of pain. This suggests that when pain is more severe catastrophizing reduces the ability to suppress or disengage from the pain, which could partly explain the transition from acute to chronic pain. A recent study supports this idea, finding an association between catastrophic thinking and increased experimental and clinical pain sensitisation, and reduced sensitivity to innocuous stimuli (Meints et al., 2019). It has also been positively correlated with temporal summation, where repeated identical pain stimuli result in an increase in pain ratings; a ‘summation’ (Granot, Granovsky, Sprecher, Nir, & Yarnitsky, 2006). Therefore, as well as being associated with CNS pain inhibition mechanisms, catastrophizing may also impact central pain sensitization processes.

Catastrophizing in the form of rumination and helplessness has been

significantly associated with phantom limb pain, accounting for 35% of the variance (Vase et al., 2011) when depression and anxiety are controlled for. This supports the link to sensitisation mechanisms. Temporal summation or 'wind-up' pain and catastrophizing activate similar areas of the brain, such as the prefrontal cortex, the somatosensory cortex, the anteria cingulate cortex and the insula and this may represent a common mechanism underlying both phenomena (Vase et al., 2011). A positive correlation was also found between catastrophizing and detection thresholds for cold and tactile stimuli (Vase et al., 2011) suggesting that catastrophic thinking may increase hypervigilance to painful events, reducing the threshold for detection and increasing pain intensity with each repeated painful stimulus. It is important to note, however, that the causal nature of these relationships has yet to be established.

Where the biopsychosocial model of pain is concerned associations have also been found between pain catastrophizing and other physiological processes (Quartana et al., 2009). One area of interest is the link between cortisol and catastrophic thinking. Low diurnal cortisol variability has been associated with higher catastrophising, suggesting a possible link between catastrophic thinking and altered activity of the HPA (HPA) axis (Johansson et al., 2008). This has been supported by a study looking at salivary cortisol responses to pain and pain catastrophising in participants with temporomandibular disorder (TMD) and in healthy participants. No difference was found in the relationship between catastrophizing and salivary cortisol concentrations between the different participant groups. However, when the groups were combined, catastrophic thinking was positively associated with raised cortisol concentration levels after pain testing (Quartana et al., 2010). The production of too much cortisol, hypercortisolism, has been associated with reduced inhibition of pro-inflammatory cytokines, which increases sensitisation to pain (Raison & Miller, 2011). This might then explain one way in which catastrophic thinking is involved in the transition from acute to chronic pain (Quartana et al., 2010). Pain catastrophizing may exaggerate pain and lead to chronic pain via the neurophysical pathway of adrenocortical responses to pain (Quartana et al., (2010). Analysis of cortisol concentration, therefore, could be a useful way to validate self-report measures of catastrophic thinking in the design of

research.

The research discussed points to a link between the modulation of the pain experience and catastrophic thinking, but it does not indicate whether catastrophizing modulates the experience of pain at a spinal or supraspinal (above the spine, the brain) level. Terry, Thompson and Rhudy (2015) carried out a study whereby they delivered pain stimuli to elicit a single nociceptive flexion reflex (NFR) and temporal summation of NFR (TS-NFR) before and after manipulating a reduction in catastrophizing. They found that a reduction in catastrophizing reduced pain intensity and unpleasantness in both the single NFR condition and the TS-NFR condition and that the reduction in pain intensity and unpleasantness was partially mediated by reduced catastrophizing. This suggests that catastrophizing not only impacts on the sensation of pain, but also on the affective aspect of pain. This study also found that a reduction in pain catastrophizing reduced TS-NFR but not NFR in response to single pain stimulations. However the effect on TS-NFR was not mediated by catatrophizing. The results of this study indicates that where pain is concerned, catastrophizing is influential at a supraspinal level rather than at a spinal level as it does not mediate spinal nociception (Terry et al., 2015).

Much of the research into catastrophic thinking and pain has focused on the able-bodied population but this association has also been found in people with SCI who experience pain. Catastrophizing has been found to mediate the effects of psychological distress and pain severity on community integration and pain interference, suggesting that the interaction of catastrophizing, pain and distress have a negative impact on disability related to pain (Ullrich, Jensen, Loesser and Cardenas, 2007). This is in contrast to findings that SCI characteristics are not consistently associated with pain-related disability and measures of pain intensity, supporting the idea that psychosocial factors have a greater role than medical factors in predicting functioning among people with spinal cord injuries who experience pain (Ullrich, Jensen, Loesser and Cardenas, 2007). This has been supported in recent studies. It was found that, having controlled for pain intensity and mobility, high pain catastrophizing was associated with higher levels of depression and pain interference and

lower well-being and positive affect (Kim, Williams, Hassett, & Kratz, 2019). Additionally, compared to a control group of people with SCI and no pain, those who had central neuropathic pain scored higher on catastrophic thinking and psychological distress (Gruener, Zeilig, Laufer, Blumen & Defrin, 2017), suggesting that it is not necessarily the trauma of the injury that causes distress, but the presence of pain. This is important because the effect of well-being on pain intensity and interference is mediated by low catastrophic thinking and not by pain medication implying that treatments aimed at targeting pain catastrophizing may be more effective than drug treatments focused solely on pain reduction (Furrer, Michel, Terrill, Jensen, & Müller, 2019).

For people with SCI living in the community, catastrophizing significantly predicts pain interference (Molton et al., 2009) and psychological distress, even when pain intensity, pain coping scores and SCI-related variables are controlled for (Turner, Jensen, Warms and Cardenas, 2002). Pain catastrophizing has also been positively correlated with pain intensity, pain interference and with mood in SCI in-patients (Nicholson Perry, Nicholas & Middleton, 2009), although more recently it was not found to predict the presence or intensity of pain three and a half years post injury (Finnerup et al., 2016). This may reflect research suggesting its impact is more concerned with other pain-related outcomes such as pain interference and distress (Turner et al., 2002).

Of additional concern is that pain catastrophizing has been associated with a greater likelihood of psychological disorder comorbidity (Craig et al., 2015) suggesting that it might increase the likelihood of more than one psychological problem occurring. Catastrophizing, therefore, is particularly problematic for people with SCI, both in hospital and in the community, but Edwards et al. (2016) note that whilst high catastrophizing has been associated with poorer treatment outcomes, there is also evidence to suggest that catastrophic thinking can be reduced by treatments such as Cognitive Behavioural Therapy (CBT; Thorn et al., 2007) and these effects have been found to persist over time (Turner, Mancl & Aaron, 2006). This reduction in catastrophizing has

been linked to better outcomes from behavioural pain treatments such as CBT (Smeets, Vlaeyen, Kester, & Knottnerus, 2006), leading to a reduction in pain intensity and improved functioning (Lazaridou et al., 2017; Miró et al., 2018). However, third-wave CBT treatments such as mindfulness can have the capacity to increase or decrease the effects of catastrophic thinking on pain outcomes, depending on the aspect of mindfulness involved. For example, whilst observance reduced the association between catastrophizing and pain, being nonjudgemental and acting with awareness magnified the effects, (Dorado, et al., 2018). As catastrophizing responds to interventions such as CBT it could be an important target for early treatment during rehabilitation following SCI, particularly if this would impact positively on rehabilitation outcomes. However, the type of CBT offered may need to be carefully matched to patients' characteristics to ensure the efficacy of the treatment (Dorado, et al., 2018).

The body of evidence supporting the role of pain catastrophizing as a mediator between psychological factors and pain-related variables, and as a predictor of pain-related outcomes is large, both in the able-bodied and spinal cord injured populations. How catastrophic thinking combines with other biopsychosocial variables to influence daily functioning in people with SCI and pain needs further research to inform the type of treatments that may prove efficacious.

6.4.2 **Pain and Acceptance**

Pain acceptance is defined as a willingness to experience pain without trying to control it, and as a process of engaging in activities despite the presence of pain, rather than judging it, focusing on solving the problem of pain and engaging in avoidant behaviours (McCracken & Vowles, 2006). A central tenet of acceptance is that individuals can continue to engage in valued activities despite the presence of pain; pain reduction is not therefore the goal in acceptance based treatment interventions. Instead, the aim is to develop psychological flexibility that enables an individual to accept that the pain is beyond their control and therefore cannot be changed (McCracken & Vowles, 2014). Therefore, it has been suggested that interventions should aim to help

the patient to change the way they frame the problem of pain and break out of the perseverance loop as described in the Problem Solving Model of pain (Eccleston & Crombez, 2007). A relatively recent model, the acceptance and commitment model (Figure 14), has developed from acceptance and commitment therapy (ACT; Hayes, Strosahl, & Wilson, 1999) and supports this approach, suggesting that an acceptance of pain could be more important than a continued focus on pain relief (McCracken & Vowles, 2006). It is unlikely that total pain relief can be achieved (Turk, Wilson, & Cahana, 2011). The focus, therefore, should be on improved functioning with less emphasis on unhelpful coping strategies (Turk, Wilson, & Cahana, 2011).

The acceptance and commitment model focuses on psychological flexibility which has six interrelated processes, and can be seen in Figure 14 below. This is referred to as the Hexaflex Model (Hayes, Strosahl & Wilson, 2012). Contact with the present moment refers to avoiding ruminating about the past and worrying about the future so as to be able to act effectively in the present. An individual needs to be clear about what they value so that those values can direct life choices and decisions. Committed action is about identifying what actions are necessary to put the values into practice and committing to those actions in a flexible but persistent way. Having the self as context refers to being able to observe ones thoughts and feelings without being attached to them or feeling the need to defend them. Cognitive defusion involves recognising that those thoughts and feelings are not factual and being able to reduce their influence. Acceptance involves being equally willing to experience both pleasant and unpleasant sensations and cognitions, especially when doing so assists in goal achievement (Yu & McCracken, 2016), and this facet of psychological flexibility is key where pain is concerned.

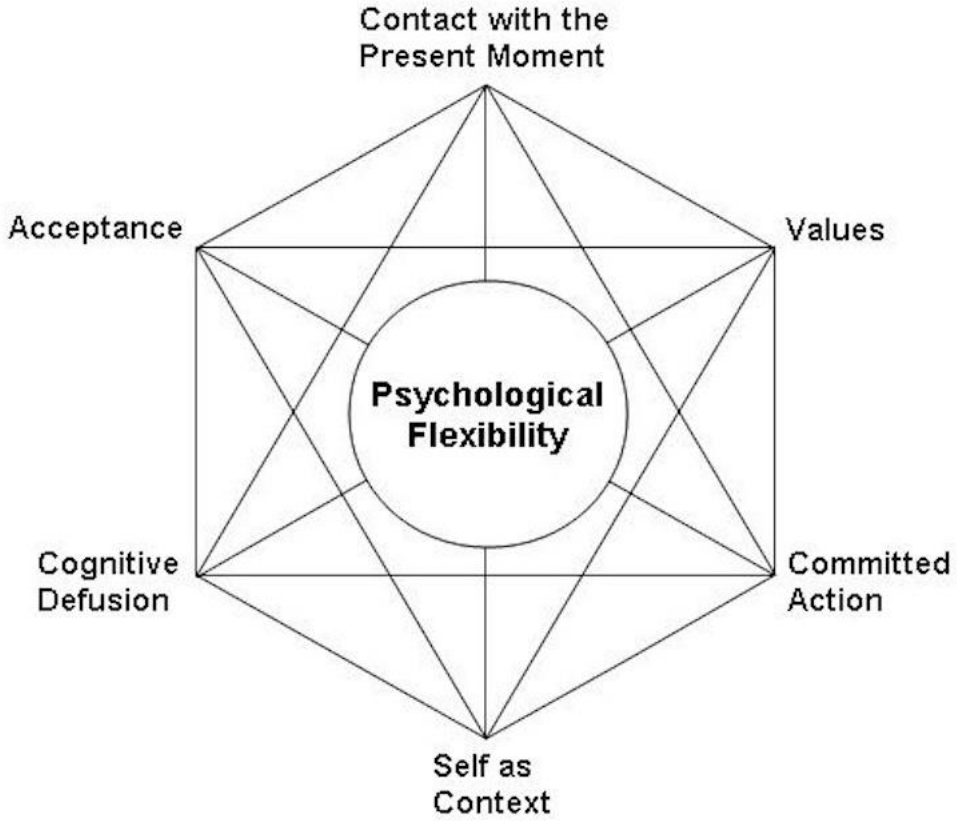

Figure 14. The Hexaflex Model of Acceptance and Commitment. See text for full description. From "*Acceptance and Commitment Therapy: The Process and Practice of Mindful Change*", by S.C.Hayes, K. D. Strosahl, and K. G. Wilson, 2012, New York: Guildford Press. Copyright 2012 by Steven C. Hayes. Used by permission.

In comparison to a coping approach, accepting pain has been found to reduce pain, emotional distress and pain-related activity and improve physical functioning (McCracken & Eccleston, 2003). It is also likely that acceptance could be an important mediator between pain-related variables such as catastrophic thinking and pain outcomes such as physical functioning, avoidance, depression and anxiety (Vowles, McCracken & Eccleston, 2008). This has also been found in the opposite direction, with a decrease in depression, anxiety and disability being associated with increased pain acceptance when changes in pain levels are controlled for (McCracken & Gutierrez-Martinez, 2011). Supporting this, earlier research has found that higher pain acceptance is related to better adaptive responses to pain (McCracken, Spertus, Janeck, Sinclair & Wetzel, 1999). Psychological

flexibility more generally, of which acceptance is an integral part, has been found to mediate the effects of ACT on a number of pain-related outcomes such as amount of analgesics prescribed, pain-related depression and anxiety, disability and number of medical visits required (Vowles, Witkiewitz, Sowden & Ashworth, 2014). This section will explore the literature that outlines the impact of pain acceptance in more detail. A focus on this is important because despite the many studies examining the role of acceptance in the pain experience for the able bodied population where pain is the primary condition, relatively few have studied the impact of acceptance when pain is a secondary condition, such as in a spinal cord injured sample. Because of this, and with its possible dual roles of predictor and mediator of pain outcomes, it is important that pain acceptance is included as one of the psychological variables in this study.

ACT suggests that continued problem solving and effortful coping can be maladaptive but this is not always thought to be the case (Van Damme, Crombez and Eccleston, 2008). It is possible that coping can be useful when considered from a motivational perspective where coping concerns the pursuit of life goals and self-regulation. Van Damme, Crombez and Eccleston, (2008) describe how coping strategies can be classified in different ways. Firstly, people can adopt active or passive coping strategies. Active strategies involve trying to control pain (not accepting it) or to continue functioning normally in spite of it (pain willingness). Passive strategies are to do with surrendering to the pain. Secondly, people can adopt approach or avoidance strategies, where engaging with the pain is viewed as an approach strategy and avoiding activities that may cause pain is an avoidance strategy. Thirdly, people can be problem-focused or emotion-focused. Problem-focused strategies involve trying to solve the problem of pain and emotion-focused strategies are demonstrated by the individual seeking support from others in order to help them deal with their own emotional response to it.

Generally, active, approach and problem-focused strategies are considered to be adaptive in contrast to passive, avoidance and emotion-focused strategies which are considered to be maladaptive (Carroll, Cassidy, & Cote, 2006; López-Martínez, Esteve-Zaragaza, & Ramírez-Maestre, 2008). However, it

could be argued that none of the strategies are more effective than another when coping with chronic pain (McCracken and Eccleston, 2003). Van Damme et al. (2008), in re-positioning coping to a motivational perspective, defined it as the attempt to continue with valued activities and pursue valued goals. Here, it is thought people take either an assimilative or an accommodative route. When individuals focus on continuing with their normal activities and goals by reducing the impact of pain they are taking an assimilative route. It might be hard to disengage from this route, with individuals persisting in their attempts to reduce the impact of pain and narrowing their focus to this one goal (Van Damme et al., 2008). This is similar to Eccleston and Crombez (2007) description of people getting stuck in a vicious cycle of worry, failed problem solving, greater distress and more problem solving in their MPM of chronic pain.

If individuals take an accommodative route they will appraise the goals they are struggling to achieve, disengage from these unattainable goals and engage in new ones that can be pursued more successfully (Van Damme et al., 2008). This approach is thought to be far more beneficial to individuals and can improve their quality of life (Wrosch, Scheier, Miller, Schultz and Carver, 2003), and therefore it implies that an accommodative route would be more adaptive, but neither one can be considered the right approach. An assimilative strategy could be adaptive to a degree but then become maladaptive. For example, persistence in goal achievement may be beneficial if the individual has accurately appraised their abilities to achieve the goal. However, if they have overestimated their abilities they may get stuck in the cycle of misdirected problem solving (Rusu & Hasenbring, 2008). An accommodative strategy is only effective if the individual has control over the goals they wish to disengage from. Disengaging too early could be likened to surrender, an avoidance strategy (Van Damme et al., 2008). In this way, coping with chronic pain could be defined as the motivation to either remove the barriers that impede goal achievement or to identify different goals that have a higher likelihood of success (Van Damme et al., 2008). It is possible that acceptance has a key enabling role to play in this, in that accepting pain as a part of life could lead to lower motivation to keep trying to solve the

problem of pain, and a greater likelihood of focusing attention on different, valued activities.

The current literature identifies two types of acceptance that have been associated with the pain experience: general psychological acceptance, which relates to the acceptance of various undesirable psychological experiences, and pain-related acceptance, which is a specific type of the former (McCracken & Zhao-O'Brien, 2010). General psychological acceptance has been found to predict levels of functioning in chronic pain patients (McCracken & Zhao-O'Brien, 2010) whilst more specific pain-related acceptance has been associated with a much wider range of pain outcomes, such as pain-related anxiety and depression, pain intensity and physical disability (McCracken & Gutierrez-Martinez, 2011). Both specific pain acceptance (Chiros & O'Brien, 2011) and general psychological acceptance though have been identified as predictors of pain catastrophizing, with individuals adopting less catastrophic thinking with regards to their pain when they have higher levels of general psychological acceptance and pain-related acceptance (De Boer, Steinhagen, Versteegen, Struys, & Sanderman, 2014). Therefore, being accepting of unpleasant psychological experiences other than just pain, may have a positive impact on pain outcomes through the mediating effect of pain catastrophizing. This is important for people with a SCI because it infers that the way they appraise their injury might be influenced by the degree to which they adopt an accepting stance. It might explain how appraisal of injury and pain experience are linked.

Acceptance is important where pain catastrophizing is concerned. A negative relationship has been found between the two (Gillanders, Ferreira, Bose & Esrich, 2012) and acceptance has also been associated with lower pain fear-avoidance, which consists of catastrophic thinking, hypervigilance and fear-avoidance beliefs (Ramírez-Maestre, Esteve & López-Martínez, 2014). It is probable that when an individual accepts their pain they are more likely to engage in valued activities and goals (Crombez, Eccleston, Van Damme, Vlaeyen & Karoly, 2012). This in turn leads to less avoidant behaviour, reducing fear beliefs, catastrophic thinking and attention to pain (Ramírez-

Maestre, Esteve & López-Martínez, 2014). In this way, lower pain fear-avoidance might explain how higher pain acceptance is associated with improved pain-related disability (Esteve, Ramírez-Maestre, & López, 2007).

Both pain catastrophizing and acceptance have been associated with various pain outcomes and both have been associated with negative affect (Craner, Sperry, Koball, Morrison, & Gilliam, 2017). However, they have been found to affect pain outcomes differently; pain catastrophizing has been found to predict higher pain intensity and acceptance of pain has predicted better functioning in activities of everyday living (Craner et al, 2017). Mediation analysis has offered some explanation of how these two processes interact to affect pain outcomes, finding that acceptance is an important influence in the relationship between pain catastrophizing and various outcome measures, such as depression, pain intensity, anxiety and physical disability (Vowles, McCracken & Eccleston, 2008). However, mediation analysis also points to differences in the way these two constructs impact on pain, with catastrophic thinking mediating the effect of pain on emotional functioning, and the relationship between pain and physical functioning being mediated by acceptance (Gillanders, et al., 2012).

This supports earlier research suggesting that acceptance is more closely related to functionality and catastrophic thinking has a stronger relationship with emotional distress (Esteve, Ramírez-Maestre, & López, 2007). However, pain catastrophizing has been found to be a stronger predictor of depression, pain intensity and pain interference, both as a predictor and as a mediator when acceptance did not predict or mediate any of these outcomes (Elvery, Jensen, Ehde, & Day, 2017). Given that acceptance has been found to correlate with both functional disability and negative affect (Craner et al, 2017) it might be seen as surprising that it is not a stronger predictor of emotional distress in these studies. It is possible that acceptance acts on pain outcomes through engagement in activities, thereby exerting greater influence on physical functioning, whereas catastrophizing exerts its influence through cognitive appraisal, having a greater effect on emotional distress. What is generally agreed is that both constructs play an important role in adaptation to

chronic pain and its outcomes (Gillanders, et al., 2012) therefore, both need to be included in research seeking to better understand the psychological influences associated with this.

It is widely acknowledged that acceptance is associated with lower pain (McCracken & Eccleston, 2003) and physical disability (Craner et al, 2017), but the literature is more mixed with regards to whether it has an effect over time. One study found that it did not explain the increase in pain and disability over a two-year period, but it did explain the progression of depression, with higher acceptance predicting lower depression even when pain levels and degree of disability increased (Pinto-Gouveia, Costa & Marôco, 2013). Depression itself has been linked to various pain outcomes (de Heer et al. 2014). Other studies have also found a link between lower acceptance and higher depression in patients with chronic pain (Costa & Pinto-Gouveia, 2013), and the relationship between pain and depression and pain and disability might be mediated by acceptance (Pinto-Gouveia, Costa, & Marôco, 2016).

This has been supported cross-sectionally and longitudinally, where pain acceptance increased in response to a three-week Cognitive Behavioural Therapy (CBT) pain management programme, and then explained the variance and predicted improvements in depression, anxiety and physical functioning at a 3-month follow-up when pain intensity and catastrophizing were both controlled for (Baranoff, Hanrahan, Kapur & Connor, 2013). It has also been found to mediate the effects of CBT on outcomes such as pain interference and depression, although there is less evidence that it affects pain intensity ratings (Akerblom, Perrin, Fischer & McCracken, 2016). This suggests that the degree to which individuals adopt an accepting approach to their pain, contributes significantly to the effectiveness of treatment, even when acceptance is not targeted specifically in the treatment programme, as it is not in CBT. When pain acceptance is specifically targeted, such as in ACT, it has been found to mediate the effect on a change in activities of daily living over a 6-month period, whereas no mediating effect of depression or anxiety was found (Cederberg, Cernvall, Dahl, von Essen, & Ljungman, 2016). This suggests that improved functioning may not necessarily require reduced pain

or improved emotion-regulation, but rather increased acceptance, and acceptance might be the mechanism by which pain management programmes, such as ACT and CBT, are effective (Akerblom et al., 2016).

Further mediation analysis implicates acceptance in the relationship between pain and disability and guilt (Serbic & Pincus, 2017), indicating that it might be an important factor in regulating emotional response. In support of this it has been found to mediate the relationship between pain interference and intensity and negative affect (Fish, McGuire, Hogan, Morrison, & Stewart, 2010). This might be because acceptance strategies are more effective in emotion-regulation than other strategies where pain is concerned (Kohl, Rief & Glombiewski, 2012). Being able to engage in activities despite the presence of pain beyond their control results in less worry, fewer avoidant behaviours and greater social contact and support (Serbic & Pincus, 2017). In this way acceptance could be used to improve various outcomes in chronic pain conditions through more effective emotion regulation (McCracken & Vowles, 2014).

The literature discussed so far has considered acceptance as a single factor but there is justification for considering the two domains of acceptance, pain willingness and activity engagement, separately. There is evidence, for example, that activity engagement might have a stronger effect on pain-related outcomes than pain willingness. It was found to have a larger mediating effect between pain intensity and pain-related distress and pain interference than pain willingness in an internet sample study validating the chronic pain acceptance questionnaire (Fish, McGuire, Hogan, Morrison & Stewart, 2010). It also had a stronger moderating effect between changes in pain intensity and changes in depression in a study of people living with long-term disability (Jensen et al., 2016). Larger effect sizes have also been found for change in activity engagement as a result of attending a cognitive behavioural pain management programme, although in this same study pain willingness had increased more at the three-month follow-up, in comparison to engagement in activities (Baranoff, Hanrahan, Kapur & Connor, 2013). This implies that it might be easier to change pain acceptance behaviourally through activity

engagement than it is to change it cognitively through pain willingness in the short term. Focusing specifically on activity engagement could, therefore, have greater benefits rather than focusing on the less observable aspect of pain acceptance. Over time, significant improvement in pain willingness may be seen as a result (Baranoff, Hanrahan, Kapur & Connor, 2013).

Very few studies have considered the role of acceptance in the pain experience of people with a SCI, where pain is the secondary condition. Those that have, support the beneficial role of acceptance, showing a relationship between pain acceptance and better quality of life, lower depression and less pain interference (Kim et al., 2019; Jensen et al., 2016; Kratz, Hirsh, Ehde & Jensen, 2013). Additionally, it has also been associated with an increase in social participation suggesting that targeting pain acceptance may be beneficial not only to pain outcomes but also to social activity engagement (Kim et al., 2019).

Benefits have also been found longitudinally with higher pain acceptance predicting function and symptom improvements over a three and a half year period, suggesting that for people with a disability, the trajectory of these outcomes might be influenced by pain acceptance (Jensen et al., 2016). Additionally, the effects of higher levels of pain on engagement in activities and on general pain interference are buffered by acceptance in people with SCI, whereby higher acceptance leads to lower interference and increased physical activity, and this has been reported on a moment-to moment basis, not just in retrospect (Kratz, Ehde, Bombardier, Kalpakjian & Hanks, 2017).

Similarly to the able bodied population, there is also evidence to suggest that for people with SCI, the two domains of pain acceptance, activity engagement and pain willingness, may predict different pain outcomes. Pain willingness has been found to predict lower depression and interference from pain, whilst activity engagement, alongside predicting these outcomes, predicts better quality of life and social role satisfaction (Kratz, Hirsh, Ehde & Jensen, 2013). It is also a much more robust predictor of adjustment than pain willingness (Kratz, Hirsh, Ehde & Jensen, 2013). This suggests that pain willingness is

more likely to affect only negative indicators of adjustment rather than both negative and positive ones, which are more associated with activity engagement. However, these subscales combined are a better predictor of pain-related outcomes than self-reported pain intensity (Kratz, Hirsh, Ehde & Jensen, 2013) and also predict lower use of pain medications such as opioids and gabapentinoids, beyond the effects of pain intensity (Kratz, Murphy, Kalpakjian & Chen, 2018). This is important because the efficacy of medication in the treatment of pain following SCI is low (Cardenas & Jensen, 2006), and it is important that other treatment options are explored.

If pain acceptance is the desired state then it is useful to know how this is to be attained for individuals with SCI. In a qualitative study exploring acceptance of neuropathic pain in people with SCI, Henwood, Ellis, Logan, Dubouloz and D'Eon (2012) identified six stages that individuals sequentially move through in order to achieve acceptance, as represented in Figure 15. Initially people sought to understand their pain but did not associate it with their injury. The unpredictability and the quality of the pain impacted on their psychosocial and physical wellbeing and not always knowing what triggered increases in pain intensity caused further distress. This led people to spend their time and energy looking for pain relief, believing a cure was possible. The focus at first was on pain medication but when a number of different drugs failed to solve the pain problem, alternative treatments were tried. The failure led to increased frustration.

This supports the MPM where it is suggested that people get stuck in a perseverance loop of seeking and trying pain solutions that don't work which increases frustration and disability and only serves to increase their motivation to find other possible pain relief (Eccleston & Crombez (2007). Although this constant seeking of pain relief is generally seen as unhelpful, it may be an important stage in moving forward with pain and the only way to reach the next phase of acknowledging pain permanence (Henwood et al., 2012). Reaching this phase was key and provided a turning point where the individuals reduced the amount of time and effort invested in seeking pain relief. How long it took to reach this stage varied amongst the participants.

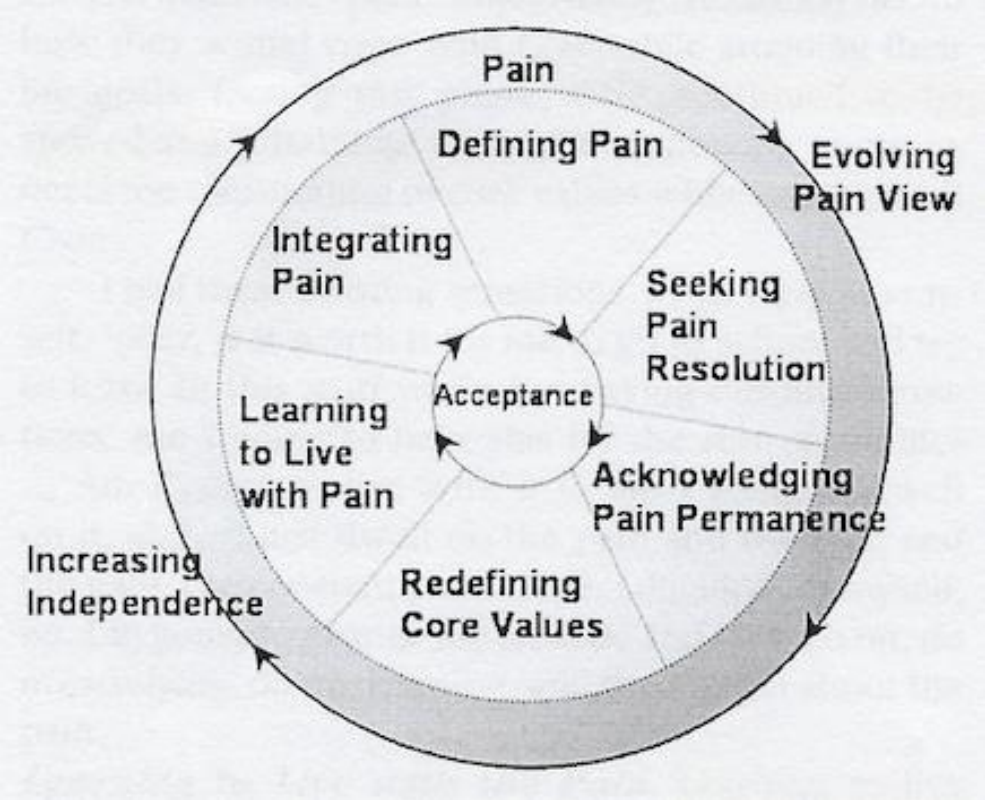

Figure 15. The process of moving forward with chronic neuropathic pain in spinal cord-injured individuals. From "Acceptance of chronic neuropathic pain in spinal cord injured persons: A qualitative approach" by P. Henwood, J. Ellis, J. Logan, C. Dubouloz and J. D'Eon, 2012, *Pain Management Nursing, 13*(4), p. 218. Copyright 2012 by the American Society for Pain Management Nursing.

Once people had accepted the permanence of their pain they spent time considering what their aspirations were for their lives and how these could be achieved in the presence of pain. At this point pain was still seen as a disabling factor but the participants made the decision to move forward in life despite it. This redefinition of core values is seen as instrumental in the ability to move forward to the next phase of learning to live with pain. This phase tended to be prolonged, challenging and the most difficult and critical. It was achieved by moving through a number of sub-processes which Henwood et al. (2012) referred to as re-programming activities. This involved changing the way they thought about pain, setting new goals and achieving them and adopting pain management strategies. The focus was on ability rather than disability which increased their sense of control. The final phase concerned integrating the pain into their lives so that it became "part of what you are"

(Henwood et al., 2012, p219). This was achieved through applying their own pain management strategies and building an active lifestyle. This lead to an improvement in coping and an acceptance of the pain.

Two processes were integral to moving forward through the phases; increasing independence, the desire of which provided the motivation to learn pain management strategies and to improve functional capacity, and an evolving pain view where the idea of pain was reframed and interpreted in a more helpful way. This enabled pain to become more bearable and it strengthened acceptance. The fact that this qualitative study and subsequent model setting out how people move forward with pain supports the quantitative research discussed above (e.g. Eccleston & Crombez, 2007) adds weight to the notion that pain acceptance is beneficial in that it reduces suffering and increases life satisfaction. Interventions, therefore, should focus on education about the unpredictability and resistance of chronic neuropathic pain to pain medication and introduce the concept of aiming for reduced suffering rather than reduced pain (Henwood et al., 2012).

Overall there is a compellingly large body of literature in the able-bodied population supporting the idea that psychological flexibility in the form of pain acceptance leads to reduced negative effect (Craner et al., 2017), less pain interference (Akerblom et al., 2016), improved physical functioning (Gillanders et al., 2012) and better adjustment (Baranoff et al., 2013). There has been much less focus on it in the spinal cord injured population, but given the evidence supporting acceptance as a positive influencer of such a wide variety of pain-related outcomes, including adjustment, it is a valuable factor to consider. Adjustment is an important part of rehabilitation for people with SCI, and anything that might impact on that needs to be researched. In the spinal cord injured literature acceptance has been found to be both an important predictor (Jensen et al., 2016) and mediator (Kratz et al., 2017) of pain-related outcomes. Further research is needed to clarify in which role acceptance is most influential in the spinal cord injured population, and this study will seek to do that.

6.4.3 **Pain and Mental Defeat**

The concept of mental defeat was originally studied in relation to Post Traumatic Stress Disorder (PTSD) and depression where it was associated with both the development and maintenance of these conditions (Ehlers, et al. 1998; Gilbert and Allan, 1998). Mental defeat is defined as "the perceived loss of all autonomy, a state of giving up in one's own mind all efforts to retain one's identity as a human being with a will of one's own" (Ehlers, Maercker and Boos, 2000, p. 45). Where pain is concerned, this refers to giving up one's will and identity to the pain. SCI can be considered a traumatic event which commonly leads to chronic pain, however, it has been suggested that only 8.8% of people with SCI have symptoms of PTSD on discharge from hospital, with this figure reducing to 2% four years post discharge (Schönenberg et al., 2014). Studies vary in their estimates considerably; Hatcher, Whitaker and Karl (2009) found that 62% of people 15 years after their SCI had PTSD whereas Krause, Saunders and Newman (2010) found less than 10% of people had PTSD on average 20 years post-injury. It is not clear why there is such disparity between the studies. It may be because of the different assessment methods used, with some studies using self-report and others using interviews, and whether a civilian or veteran sample was used (Schönenberg et al., 2014). Importantly, it can be concluded that SCI is significantly associated with psychological distress and post traumatic stress (Schönenberg et al., 2014). There have been few, if any, studies looking at SCI and mental defeat but given that both are associated with PTSD, depression and chronic pain (Tang, Salkovskis and Hanna, 2007) there is a justification for including it in this research.

As PTSD and depression are both comorbid with chronic pain (McWilliams, Cox & Enns, 2003) there has been a natural interest in the role mental defeat may have in this condition. In a study to investigate this Tang, Goodchild, Hester and Salkovskis (2010) asked 133 pain patients at a pain clinic to each complete ten questionnaires; four measuring pain interference, distress and disability and six measuring primary psychological predictors such as pain catastrophising, mental defeat, anxiety and rumination. They found that mental

defeat correlated with poor sleep, depression, pain interference, anxiety, functional disability and psychosocial disability. Medium to strong effect sizes were found when they looked at between group differences of those with high scores and those with low scores on measures of mental defeat, possibly explaining the differences in individual functioning in people with chronic pain, and demonstrating the way in which disability develops (Tang et al., 2010). This could be particularly relevant where depression is concerned. In patients with major depression, symptoms of depression and perceptions of defeat correlate even when hopelessness is controlled for (Gilbert and Allan, 1998). Depression is strongly associated with chronic pain. These results support the idea that, as well as being found in people with PTSD and depression, mental defeat is also strongly associated with chronic pain (Turner-Cobb, Michalaki, & Osborn, 2015).

Where chronic pain is concerned, mental defeat can be thought of as the way in which people make negative appraisals or form negative beliefs about themselves in relation to the pain (Tang, et al., 2007). This is triggered by the chronic pain and determines how disabling they experience the pain to be. It also causes attention to focus on the negative aspects of the pain experience and can interfere with coping ability, supporting the cognitive-affective model of attention to pain (Eccleston and Crombez, 1999). A recent study concurs with this as mental defeat was associated with affective pain and with pain-related self efficacy (Hezeldene-Baker, Salkovskis, Osborn, & Gauntlett-Gilbert, 2018). It is likely, therefore that chronic pain patients who experience mental defeat will also experience greater symptom severity in terms of pain, and greater disability (Tang et al., 2010).

It has been reported that up to 25% of people who attend pain centres have self-harmed or attempted suicide (Okifuji & Benham, 2011) and that existing psychiatric conditions such as depression have been identified as risk factors. It is possible that the presence of mental defeat may also be predictive of self-harm or suicidal ideation (DeCaria & Patel, 2018; Tang, Beckwith and Ashworth, 2016). This idea has been supported, with mental defeat identified as a better predictor of suicidal intent than anxiety, depression and pain

catastrophising, but it only predicted the participants worst ever intent and not their present intent (Tang, et al., 2016). This was independent of the effect of pain intensity, which suggests that mental defeat is an important factor when considering the risk of self-harm and mental well-being of people experiencing chronic pain. More recently, a comprehensive review of the risk factors associated with suicidality in people with chronic pain found that not only was mental defeat one of the key variables, but also being disabled (Racine, 2018). This implies that for people with SCI and pain who experience mental defeat the risks may be even greater.

Mental defeat is closely associated with other psychological disorders, particularly when these are comorbid with chronic pain. Patients suffering from chronic pain have been found to score higher on measures of depression and anxiety than control groups without a pain condition (Tang et al., 2007) leading to the possibility that mental defeat is a manifestation of one of these mood disorders. However patients with chronic pain attending a pain clinic have scored higher on the Pain Self Perception Scale (PSPS), which measures mental defeat, than chronic pain volunteers (not receiving treatment) even when they were matched in depression and anxiety scores, and when pain and mood disturbances were controlled for (Tang et al., 2007). This would not be expected to be the case if mental defeat represented the same construct as depression and anxiety and it supports earlier research findings that when people are experiencing psychological distress, they are more likely to seek treatment for the pain (Ziegler & Paolo, 1995). Additionally, chronic pain patients scored higher on the PSPS than anxiety patients, with only a moderately strong relationship between mental defeat and anxiety and mental defeat and depression (Tang et al., 2007). Altogether, this suggests that mental defeat is distinct from other mood disorders and should be explored as a separate factor that contributes to the pain experience (Hezeldene-Baker, et al., 2018).

The association between mental defeat and pain-related outcomes has been found across different cultures. In a study of mental defeat in a Hong Kong Chinese chronic pain sample, mental defeat predicted depression, anxiety and

pain interference independent of the effect of pain severity (Tang, Shum, Leung, Chen and Salkovskis, 2013). This supports the idea of mental defeat being distinct from depression and anxiety and it indicates that mental defeat might affect pain outcomes through the mediation or moderation of poor mental health. In a comparison of previous studies that explored the relationship between mental defeat and other psychological factors (Cheun et al., 2008; Lim et al., 2007; Yap, et al., 2008), it was found that mental defeat had stronger correlations with both the depression and anxiety scales of the Hospital Anxiety and Depression Scale (HADS) and with the pain Numerical Rating Scale (NRS) than did pain catastrophising or pain acceptance supporting this suggestion.

Further endorsement of the relationship between mental defeat and psychological disorders was found in a systematic review of the literature examining the associations between defeat and entrapment and the common mental health disorders of depression, anxiety, posttraumatic stress disorder and suicidality. There was a particularly strong positive association between defeat and depression (Taylor, Gooding, Wood & Tarrier, 2011). More recently, a meta-analysis to assess the size and consistency of these relationships, and whether these relationships were more robust in some cases than in others, found strong relationships between defeat and entrapment and each of the psychiatric conditions, with a particularly large association between defeat and depression (Siddaway, Taylor, Wood and Schulz, 2015). This is consistent with the theory that individuals have an innate, adaptive response to perceived defeat called the Involuntary Defeat Strategy (IDS; Sloman, 2000). This is activated when competition for meaningful resources is high, and aims to limit possible resulting damage from such conflict by demonstrating a non-threatening position and ceasing activity towards unachievable goals, thus reducing excessive costs.
Where depression is concerned, it is theorised that an inappropriate or dysfunctional response from the IDS causes psychological disorders (Sloman, 2000). Whilst comparative non-human studies indicate that reduced social rank causes the defeat that leads to depression (Shively, Later-Laird, & Anton, 1997; Shively, et al., 2005), in humans a sense of defeat may derive from a

failure or loss of a more diverse range of goals or aims (Taylor et al. 2011). Examples of these may include losing valued social and material resources, attacks or put-downs from others, or self-criticism and striving for unachievable goals (Gilbert, 2000), as in the MPM of pain (Eccleston & Crombez, 2007).

This is important where SCI is concerned because the severity of the injury inevitably involves some form of loss, whether this be the reduced ability to achieve sporting goals, reduced income if the injury is particularly severe or the sense of loss of the life a person had been leading prior to the injury (Dickson, Allan, & O'carroll, 2008). This suggests that a sense of defeat could be a particularly salient experience for some people with this type of injury, and more so if pain is also a factor because of the possibility of increased disability which might result in a greater perception of loss. Tang et al. (2010) suggest that mental defeat could provide a further explanation of the misdirected problem-solving model of chronic pain (Eccleton & Crombez, 2007). People experiencing pain might be motivated to continue trying to escape it because of the increased sense of loss they feel, caused by the pain-related feelings of defeat. It is possible that experiencing repeated failures to solve the problem of pain then leads to further mental defeat, causing people to become stuck in the perseverance loop. In this context they conceptualise it as a failed struggle, resulting in disability and distress (Tang et al., 2010).

Because it should be possible to change perceptions of struggle and defeat, it is important that these concepts are considered in pain management treatment programmes. However, correlations between greater pain severity, mental defeat and lower educational achievement, suggest that a lower education level might moderate the development of mental defeat (Tang et al., 2013). If this is the case, then pain management programmes need to be designed in such a way as to be accessible to people with a variety of academic backgrounds.

Mental defeat is not only distinct from depression and anxiety, but is also distinct from catastrophising. It has been found to predict pain interference,

depression and psychosocial disability, whereas catastrophising predicts sleep interference, anxiety and functional disability (Tang et al., 2010). Catastrophising and mental defeat combined to explain the variance in three out of six of these disability measures suggesting that they may be related but the fact that they each predicted different measures means they should not be considered to be the same thing. Mental defeat may be a form of catastrophising but, rather than the focus being on the experience and meaning of pain as it is generally when catastrophising occurs, there is an internal focus on the effects of pain on a person's life and identity (Tang et al., 2007). The relationship between mental defeat and catastrophising might be a reciprocal one, with mental defeat leading to greater catastrophising over milder pain experiences and these negative appraisals in turn leading to an increase in mental defeat (Tang et al., 2007). This could lead to a reduction in tolerance to pain and a lowering of the pain threshold and might, therefore, mediate the progression from acute to chronic pain (Tang et al, 2007). This is particularly important in a spinal cord injured population where pain interferes with rehabilitation and adjustment to the injury.

This type of bidirectional relationship could also be found between anxiety and depression and defeat and entrapment (Griffiths, Wood, Maltby, Tayor and Tai, 2014). Very little previous research had investigated longitudinally whether defeat and entrapment would predict anxiety and depression, nor had this been studied the other way round, where anxiety and depression predict defeat and entrapment. A one-year longitudinal study investigating these relationships found that higher levels of mental defeat and entrapment at the first assessment point predicted higher scores on anxiety and depression scales at the second time point. Also, high anxiety and depression scores at time one predicted higher mental defeat and entrapment one year later (Griffiths et al., 2014). This suggests that these psychological variables may have a reciprocal relationship. Depression and anxiety might lead to feelings of defeat and entrapment, which in turn increase psychological suffering in the form of depression and anxiety.

In addition to psychological variables, an individuals socioeconomic status

may make them either more or less at risk of experiencing mental defeat. Individuals from low socioeconomic backgrounds might be particularly vulnerable to experiencing mental defeat as they may feel more trapped by their situation, with fewer opportunities to escape (Griffiths et al., 2014). This might be because socioeconomic deprivation has been linked to reduced job opportunities (Department for Communities and Local Government, 2011), poorer general health (Adler et al., 1994), and higher rates of mortality (Department of health and Social Security, 1980). People with a SCI are faced with similar challenges (Middleton et al., 2012; Krause, Saunders, & Acuna, 2012; Cao, Krause, & Dipiro, 2013) suggesting that they too may be more susceptible to experiencing mental defeat.

To conclude, mental defeat has been associated with pain intensity and pain disability (Turner-Cobb, et al.,2015; Tang et al., 2010). It is thought to have a reciprocal relationship with catastrophising (Tang et al., 2007) and also with depression and anxiety (Griffiths et al., 2014) and has been found to predict suicidal ideation in people with chronic pain (Tang et al., 2016). Little, if any, research into SCI and mental defeat has been carried out. Given that mental defeat is so closely linked to pain and various psychological variables, and that it is possible that people with a SCI may be at higher risk of experiencing mental defeat, it is important that research considers the impact that mental defeat may have for people with SCI. If it is shown to be detrimental to well-being in this population, measures to reduce it can be included in pain treatment programmes.

6.4.4 **Pain, Depression and Anxiety**

This section explores the relationship between pain (neuropathic and nociceptive) and mental health problems, specifically anxiety and depression. These two disorders are of interest because they are the most commonly reported mental health problems in England (The Health and Social Care Information Centre, 2009). Additionally, the treatment of these conditions has been strongly associated with a reduction in pain severity (Zanini, Voltolini, Gragnano, Fumagalli, & Pagnini, 2018). A high comorbidity between

depression and anxiety has been reported, with 75% of people with depression also suffering from an anxiety disorder and 81% of people with an anxiety disorder also having a comorbid depressive disorder (Lamers et al., 2011). Both of these psychological problems have been strongly associated with pain, with individuals who experience pain being significantly more likely to suffer from depression and/or anxiety (Carleton et al., 2018), and pain-related anxiety being associated with opioid misuse (Rogers et al., 2018). For these reasons it is important to consider both types of disorder rather than focusing only on one or the other. Literature exploring diagnosed mental health problems and literature that has explored indicators of sub-clinical depression and anxiety (symptoms which are not severe enough to meet the diagnostic criteria for these disorders) and correlational associations between these and pain have been included. It is important to identify these relationships to ensure that the mental health needs, diagnosed or undiagnosed, of people with a SCI are not overlooked when designing treatment plans.

Studies reporting the prevalence rates for comorbid pain conditions and anxiety disorders suggest that people with persistent pain problems are at greater risk of anxiety than the general population, and that GAD is associated with increased pain severity (Csupak, Sommer, Jacobsohn, & El-Gabalawy, 2018). However, there is disparity in the literature as to the extent of comorbidity. One review of the literature found that between 20% and 70% of panic patients experienced chronic pain (Asmundson and Katz, 2009) whereas, in a cross cultural study into pain and mental disorders, a prevalence rate of between only 1% and 8% for GAD and 1% and 9% for Panic Disorder was reported (Gurege et al., 2008). This disparity is also seen in the literature where depression and pain is concerned. In a literature review to determine the prevalence of depression in people with pain and the prevalence of pain in people with depression it was found that 52% of persistent pain patients suffered from low mood (Bair, Robinson, Katon & Kroenke, 2003). In contrast Gurege et al. (2008) only found a prevalence rate of between 3% and 19%.

This disparity is likely to be caused by the different population targeted by

Gurege et al.'s (2008) study which came from the World Mental Health Surveys across 17 countries. The study focused on people in the community whereas most studies, focus on people attending pain clinics or seeking treatment for their pain. It is reasonable to expect that emotional distress might be greater amongst that population than amongst people who do not perceive that they require treatment. Another explanation for the disparity, as the authors acknowledge, is that Gurege et al. (2008) used standardised diagnostic measures whereas most studies use scales measuring symptoms (e.g. HADS, Zigmond & Snaith, 1983) that are not able to provide a psychiatric diagnosis aligned to the psychiatric classification system of the Diagnostic and Statistics Manual of Mental Disorders (American Psychiatric Association, 2013). This has been supported in a sample of chronic pain patients with either neuropathic pain or fibromyalgia. Despite there being significantly more mental distress than in a healthy control group, only 7.1% met the diagnostic criteria for depression and 3.3% met the diagnostic criteria for anxiety.

Further evidence has come from a large study looking at the recurrence of anxiety and depressive disorders in 1,122 people with a history of either or both of these conditions, and what the risk factors of recurrence might be (Gerrits et al., 2014). Under examination was the degree to which chronic disease and pain symptoms are associated with such recurrence and whether subthreshold anxiety and depressive symptoms, those symptoms that do not meet the threshold criteria for psychiatric diagnosis of the disorder, mediate the association. A relationship was found between pain and depression, which was mediated by subthreshold depressive symptoms (Gerrits et al., 2014). This suggests that it is pain rather than chronic disease that increases the risk of depression and that the presence of subthreshold depressive symptoms may make a patient particularly vulnerable. Additionally, as well as diagnosed depression being associated with the onset of new pain symptoms (Sheffler, Bekelman, Schmiege, & Sussman, 2018), remitted depression and anxiety have been linked to more severe pain and disability suggesting that having a remitted mental health problem was not the same as having no mental health problem where pain is concerned (De Heer et al., 2014). This suggests that depression does not have to be current or at clinically significant levels to be

linked to greater pain intensity and pain disability. It is conceivable that this would also be the case for people with a SCI and, therefore, further research focusing on the link between pain and depressive symptoms in this population would extend the knowledge base and inform rehabilitation plans.

In a major review of the literature, Bair, Robinson, Katon, and Kroenke (2003) were interested in whether the presence of pain affected a diagnosis of depression and whether it affected depression outcomes such as the efficacy of treatment and quality of life. Additionally, they examined whether the presence of depression affected similar outcomes in people being treated for pain conditions. They found that the prevalence of pain and depression are higher when the other condition is present than when each condition is considered individually. More recent research continues to find a positive relationship between depression, anxiety and pain (Pinheiro, Morosoli, Colodro-Conde, Ferreira, & Ordoñana, 2018). It has also been noted that the pain-depression relationship has a reciprocal nature whereby the presence of depression is associated with poorer treatment outcomes for pain patients with higher pain intensity and longer pain duration. In turn, the severity of depression is found to be greater with increased pain and when pain interferes with daily activities (Bair et al., 2003). Overall, Bair et al. (2003) found that comorbid pain and depression has a poorer prognosis compared to either condition individually. It has also been suggested that depression mediates the relationship between pain and frailty implying that experiencing both conditions may result in greater disability than having either pain or depression in isolation (Xiaoyu, 2018). It is, therefore, important to understand the relationship between pain and mental health if treatment options are to address the problems effectively and result in a positive outcome.

The bidirectional association between pain and depression has been supported more recently with estimates that up to 70% of people diagnosed with depression or anxiety disorders also experience chronic pain, with pain impacting negatively on the severity of depression and depression impacting negatively on pain intensity and treatment outcomes (de Heer et al., 2014). This is important because people tend not to mention their depression, but

simply refer to their physical problems so the depression remains undiagnosed and untreated (Bair et al. 2003). It is thought the problem of undiagnosed depression in people experiencing pain is widespread, with estimates suggesting that 35% of people with pain and no psychiatric history may have depression (Lee, Choi, Nahm, Yoon & Lee, 2018).

There are few studies that have explored why people focus on somatic problems rather than their mental health but it is possible that the painful symptoms are more salient and patients may think that they indicate an underlying medical illness (Bair et al. 2003). They might believe their low mood is merely a symptom of the pain they feel and one that will improve once the pain is successfully treated. Even when depression and anxiety are recognised and treated, the existence of pain leads to poorer treatment outcomes and a longer time before remission than when no pain is present (Gerrits, et al., 2012). This comorbidity can also impact on the severity of both conditions as a strong positive relationship exists between severity of mental health symptoms and severity of pain and pain-related disability (De Heer et al., 2014).

What the research cited so far fails to address is what causes the association between pain and depression. The Örebro Behavioural Emotion Regulation Model (Linton and Bergbom, 2011) was proposed as a means of understanding the role that catastrophizing and emotion regulation might have in relapses of pain and depression.

Permission for inclusion not obtained.

Figure 16. The Örebro Model of Behavioural Emotion Regulation for Pain which highlights the role of catastrophizing, negative effect and emotion regulation in relapses of pain and/or depression. Note that there are two vicious circles whereby catastrophizing increases negative emotion and more catastrophizing (pink arrows), increasing the likelihood of relapse, and a second which underscores that a relapse is linked through learning to the trigger and in turn linked to emotion regulation making a relapse more probable in the future. From "Understanding the Link Between Depression and Pain" by S. J. Linton and S. Bergbom, 2011, *Scandinavian Journal of Pain, 2,* p. 52. Copyright 2011 by Elsevier B.V.

As depicted in Figure 16, this model suggests that a flare up of low mood and/or pain triggers a cycle, whereby catastrophizing and negative emotions, followed by a failure to regulate those emotions, leads to a relapse of depression and pain-related disability triggering further catastrophizing. If positive emotion regulation is achieved then relapse is avoided. It is the repeated unsuccessful attempts at regulating emotions that mediate the process from acute to chronic pain conditions. Learning plays a role because when negative emotion regulation leads to further pain flare-ups, the association between mood and pain is reinforced, making it more likely that catastrophic worry will be triggered, perpetuating the vicious cycle (Linton and Bergbom, 2011). Rather than being an outcome, in this model depression and pain are the stimuli that trigger catastrophizing, which in turn leads to increased disability. If the model is accurate it provides support for the idea that pain and depression need to be treated as separate problems and early on in order to avoid the cycle becoming established.

It has been suggested that catastrophising and depression both have a role in the severity of chronic pain and the disability associated with it, and that this might mean that chronic pain patients are not a homogenous group, but that subgroups exist (Borsbo, Peolsson and Gerdle, 2009). In a study looking at the degree to which the factors depression, anxiety, catastrophising, the degree of pain intensity and duration impacted on perceived quality of life and disability, four different groups of chronic pain sufferers were identified (Borsbo et al., 2009). People in the ‘most favourable’ group had low scores on depression, anxiety and catastrophising scales and reported low pain intensity and short pain duration. This group had high quality of life and low disability scores. The second group, ‘long-time / favourable’, also had low depression, anxiety and catastrophising scores but they had high pain intensity and long pain duration. Like the first group, they had a high quality of life score and low disability scores. The third group, ‘short-time / worse’, had high depression, anxiety and catastrophising scores, short pain duration and intermediary pain intensity. They had high disability scores and their perceived quality of life was

low. The final group, ‘worst off’, had the highest scores of all groups on depression, anxiety and catastrophising and also the highest pain intensity and a long pain duration. This group had the highest disability scores and the lowest perceived quality of life.

These results imply that patients with chronic pain are not a homogenous group and that it is the psychological factors that impact negatively on disability and perceived quality of life rather than the intensity of the pain or the pain duration. This was particularly the case for depression. The higher the depression, anxiety and catastrophising scores, the lower the perceived quality of life and the higher the disability. Also, high pain intensity and long pain duration did not necessarily result in higher depression, anxiety or catastrophising scores as shown by the ‘long-time / favourable’ group (who scored low on the psychological variables and high on pain intensity and duration) and the ‘short-time worse group (who scored high on the psychological variables, low on pain duration and had lower pain intensity). The results suggest that even if people suffer from a high level of pain, for a long time, if they are mentally healthy they can have a relatively good quality of life (Borsbo et al., 2009). This supports Linton and Bergbom (2011) in identifying depression, anxiety and catastrophising as being important factors in chronic pain.

What is less clear is why some people might maintain good mental health despite having chronic pain. A diathesis stress model may offer one explanation in that some people might adopt more successful coping strategies than others and so be able to cope with living a life in pain (Borsbo et al., 2009). In order to better understand these relationships it is necessary to explore how one might mediate each of the others to affect people’s perception of pain severity and their level of pain related disability. Mediation refers to the way in which the impact of one variable operates on another through an intervening variable; it explains why the impact of one variable on another exists. Mediation analysis therefore, could shed further light on the way biopsychosocial factors interact to influence pain-related outcomes.

Some studies have found that people with multi-site pain are at greater risk of depression than those with single-site pain and that people with more than one mental health problem are likely to experience greater pain-related disability than those with a single mental health problem. In a large study of over 8000 participants from the National Comorbidity Survey, which had investigated the prevalence of psychiatric disorders in the US population, the associations between mood and anxiety disorders and chronic pain were explored (McWilliams, Cox and Enns, 2003). The results were consistent with previous research, finding that the chronic pain group had higher rates of both anxiety and mood disorders than a comparison group. It was also found that people with more than one psychiatric disorder reported greater disability whereas there was no association when only one psychiatric disorder was present (McWilliams et al., 2003). This implies that those people with more severe mental health problems are likely to experience greater pain related disability, whereas a single psychiatric disorder will not necessarily impact on this. Whilst this would seem to be at odds with most research in this area, it is important to note that high comorbidity between depression and anxiety has been found, (Lamers et al., 2011). The results obtained from studies that measure only for depression or only for anxiety might, therefore, actually reflect the existence of more than one psychiatric disorder.

The research discussed so far points to the fact that individuals with a mood disorder are more likely to have chronic pain than people without a mood disorder, and that having more than one mental health diagnosis increases the risk. It is also the case that having multisite pain escalates the likelihood of having a psychological disorder. The number of pain sites has been positively associated with the risk of having a major depressive disorder or bipolar disorder classification (Nicholl et al., 2014). This supports earlier research which found that pain at a single site was significantly related to mental health problems but that those people experiencing pain at more than one location had almost double the risk of mood and anxiety disorders (Gureje et al., 2008). These studies suggest that the more pain sites and the more mental health problems an individual experiences, the more vulnerable they will be to greater disability and low mood.

Recently, the focus of research has turned to the shared physiological aspects of depression and pain. For example, it has been identified that pain and depression have common pathophysiological features such as abnormal serotonin and dopamine transmission (Goldenberg, 2010; Han & Pae, 2015), shared genetic aetiology (Pinheiro et al., 2018) and pro- and anti-inflammatory cytokine genes have also been associated with both chronic pain and depression (Illi et al., 2012; Han & Pae, 2015). Further supporting evidence was provided by the finding that concentrations of the pro-inflammatory cytokines interleukin-6 and tumor necrosis factor (TNF) were significantly higher in depressed participants than in non depressed participants (Dowlati et al., 2010). This suggests that depression involves the activation of the inflammatory response system as these cytokines are key components of that process. The inflammatory response system is normally activated by injury or illness.

A biological link between pain and depression has also been reported in a literature review concerning the comorbidity of pain and depression (Bair et al., 2003). This suggests that there is a central pain modulating system (for a more in-depth explanation of the brain structures involved see Appendix 1). Pain signals are carried by axons from the dorsal horn in the spine, via the spinothalamic tract, to the ventral posterolateral (VPL) nucleus of the thalamus and then on to the somatosensory cortex and the frontal cortex. The central pain modulating system is able to amplify or dampen these pain signals, causing more or less attention to be focused on them. The dampening effect occurs via a descending pathway from the limbic structures (the amygdala and hypothalamus) and the frontal cortex, which send messages through the periaqueductal grey (PAG). The PAG stimulates the firing of neurons in the nucleus raphe magnus (NRM), a serotinergic nucleus in the medulla. This in turn fires inhibitory neurons descending in the spinothalamic tract, inhibiting nociceptive neurons in the dorsal horn and thus reducing the individual's perception of pain (Bair et al., 2003).

In their review of human imaging studies, Ossipov, Dussor and Porreca (2010)

support this idea of a descending pain modulatory system. As shown schematically in Figure 17, they suggest that nociceptive signals ascend through the spinal dorsal horn and the spinothalamic tract to the thalamus, depicted by the red line in the diagramme. Projections are also sent to the dorsal reticular nucleus (DRt), the rostral ventromedial medulla (RVM) and the PAG. Information from the thalamus is sent to various cortical sites and to the amygdala. Nociceptive signals also ascend from the brainstem and spinal cord to the central nucleus of the amygdala (CeA) and on to the thalamus and cortical areas providing the conscious experience of pain.

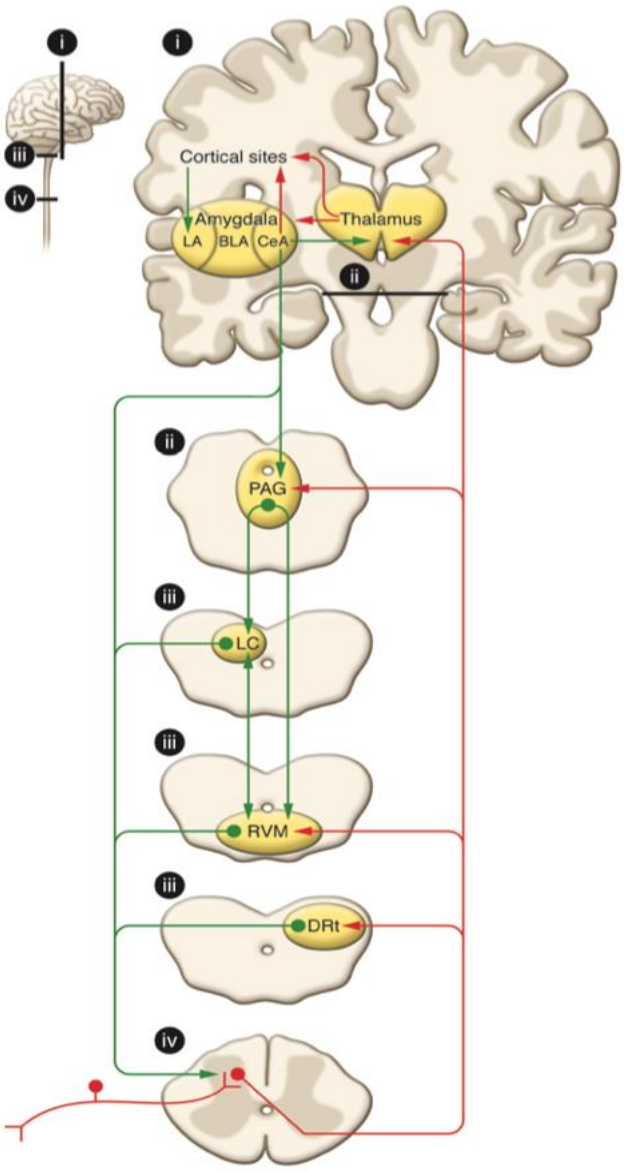

Figure 17. Pain Modularity Circuit. LA = lateral amygdala; BLA = basolateral amygdala; CeA = central nucleus of the amygdala; PAG = periaqueductal grey; LC = locus coeruleus; RVM = rostral ventromedial medulla; DRt = dorsal reticular nucleus. Areas labelled i-iv in the large diagram correspond to labels in the small diagram. Adapted from "Central Modulation of Pain" by M. H. Ossipov, G. O. Dussor, and F. Porreca, 2010, The Journal of Clinical Investigation, 120(11), p. 3780. Copyright 2010 by The American Society for Clinical Investigation.

Descending pathways, also shown in figure 17, (in green) project from the cortical areas to the lateral (LA) and basolateral (BLA) amygdala and on to the PAG. The PAG mediates pain modulation by sending inputs to the locus coeruleus (LC) which sends noradrenergic inhibitory signals to the spinal cord and projections to the RVM. The RVM modulates nociceptive inputs, either inhibiting or amplifying them, providing an autogenous pain regulatory system (Ossipov et al., 2010).

Depression has been associated with reduced levels of serotonin and noradrenaline (Han & Pae, 2015; Ruhe, Mason & Schene, 2007; Cowen, P.J., 2008), two neurotransmitters that are central to the dampening effect of the pain modulation system (Bair et al., 2003; Ossipov et al., 2010). With depleted levels of these neurotransmitters, the pain modulating system is less effective and minor pain signals may be more noticeable. This would explain why depression is associated with increased attention, multiple pain symptoms, and negative affect (Bair et al., 2003), further highlighting the need to take mental health into account when considering pain treatments.

The link between chronic pain, anxiety and depression is important where SCI is concerned because it has been found that both conditions are more prevalent in that population than in the able bodied population (e.g. Kennedy & Rogers, 2000; Ullrich, Jensen, Loeser & Cardenas, 2007; Battalio, Glette, Alschuler, & Jensen, 2018), all persist over time (Finnerup et al., 2016), and psychological difficulties cause more problems for people with SCI and pain than other factors (Tran, Dorstyn & Burke, 2016). For example, individuals with depression have a 78% risk of suicide, which decreases to 50% six months following discharge from hospital (Craig et al., 2015). Comorbidity is

problematic in SCI because it is associated with poorer functional recovery and the requirement for a greater length of time in hospital following the injury (Mehta et al., 2018). The presence of pain and depression also impacts negatively on quality of life, partly because it reduces participation in activities and in satisfaction with activities that are engaged in (Müller et al., 2017). It has been reported that whilst in rehabilitation 30% of people with SCI are at risk of experiencing a depressive disorder. This falls slightly to 27% for those living in the community (Craig, Tran and Middleton, 2009). However, a more recent meta-analysis found a mean prevalence rate for depression is 22.2% (Williams & Murray, 2015).

People with SCI also have a greater risk of having an anxiety disorder, with prevalence estimated at approximately 30% (Kennedy & Rogers, 2000; Le & Dorstyn, 2016), and feelings of helplessness (Craig et al., 2009). In general the prevalence rates of any psychological disorder is three times higher in the spinal cord injured population than in the general community and these rates do not change up to one year post-injury (Craig et al., 2015). Similarly, rates of comorbidity are also higher amongst people with SCI than amongst the able-bodied population (Craig et al., 2015). The high rates of prevalence for psychological disorders gives cause for concern, particularly as they persist through the transition to the community, and have been associated with an increased risk of pain medication misuse in the spinal cord injured population (Clarke, Cao, & Krause, 2017). In addition, high levels of depression and anxiety are associated with greater pain intensity and an increased likelihood of catastrophic thinking, with these also worsening on transition to the community (Craig, Guest, Tran, Nicholson Perry & Middleton, 2017). Further analysis of the occurrence of these difficulties following discharge is necessary to determine what support structures might need to be in place in the community for people with SCI.

It had been questioned as to whether depression, personality characteristics and personality disorders could predict disability in spinal cord injured pain patients. However, although a diagnosis of depression was predictive of disability in pain patients, personality characteristics and personality disorder

were not (Ericsson et al., 2002). The fact that depression predicted pain disability in people with SCI such a long time after the initial diagnosis suggests that these problems are enduring. This is supported longitudinally. In a sample of people with SCI seventeen years post-injury it was common to find a co-occurrence of depression and pain. This comorbidity was associated with a greater severity and greater persistency of both conditions, and people were more likely to seek support and treatment from specialised SCI centres (Ullrich et al., 2013). A more recent longitudinal study also found that increased anxiety was associated with lower satisfaction with social roles, poorer physical functioning over time, and increased pain (Battalio et al., 2018). This suggests that the comorbidity of psychological disorders and pain can interfere with rehabilitation, causing a greater and longer term dependence on SCI health professionals.

The association between depression and pain after a SCI has been well documented (e.g. Craig, Tran and Middleton, 2009; Nicholson Perry, Nicholas, Middleton and Siddall, 2009; Norrbrink Budh and Österäker, 2007). Tate, Forchheimer, Karana-Zeberi, Chiodo and Thomas (2013) were interested in this association for inpatients with traumatic or non-traumatic SCI / disease and how this might link to patient characteristics and neurological impairment. They looked at the medical records of 100 newly admitted patients at a rehabilitation unit, analysing their depression and pain ratings, neurological classification, aetiology of the SCI or disease, and demographic details. They expected that higher levels of depression at the time of admission would correlate with higher pain severity, however, although there did seem to be a trend in this direction, Tate et al. (2013) did not find a statistically significant relationship between these two variables. This supports research into pain and depression in the able bodied population (Borsbo et al. 2009) where high pain intensity and long pain duration did not necessarily result in higher depression, anxiety or catastrophizing scores and it was psychological distress rather than pain intensity that reduced perceived quality of life.

Where SCI is concerned, these findings are supported by a study exploring the impact of pain on quality of life and the influence of psychological factors

on pain (Wollaars, Post, van Asbeck and Brand, 2007). It was found that psychological factors rather than pain severity had the strongest association with quality of life, and catastrophizing and SCI helplessness were the strongest predictors. Similar results have been achieved when looking at life satisfaction in people with SCI and pain. Neither neuropathic or nociceptive pain intensity are related to quality of life (Richardson et al., 2016), whereas anxiety and depression, rather than pain, were predictive of the lower levels of life satisfaction found in participants (Norrbrink Budh and Österåker, 2007). This indicates that for people with SCI, as well as the able bodied population, when pain is reported it is important to assess for mental wellbeing as well as physical pain when considering disability and life satisfaction. This is particularly important given that people with a SCI who attended a tertiary pain clinic experienced poorer mental health than others in the community both with and without pain (Nicholson Perry et al., 2009). The implication is that people who report their pain to health professionals may be experiencing greater psychological distress than those who do not seek treatment which makes it even more important that people reporting pain are screened and treated for mental health problems.

6.5 **Conclusion**

In conclusion, anxiety and depression can increase pain intensity (Linton & Bergbom, 2011; Csupak, Sommer, Jacobsohn, & El-Gabalawy, 2018; Zanini, Voltolini, Gragnano, Fumagalli, & Pagnini, 2018), aid the development of disability (Xiaoyu, 2018), and are associated with poor treatment outcomes, especially if depression was present before treatment (Pincus, Burton, Vogel & Field, 2002). Depression can also predict disability in chronic pain patients in the longer term (Ericsson et al., 2002). Where SCI is concerned, the associations between pain and depression, anxiety and pain catastrophizing have been well documented, with key studies emerging from the UK, across Europe, North America and Australia. Psychological difficulties are the most frequently reported problems associated with pain in this population (Tran, Dorstyn & Burke, 2016). Fewer studies have considered the role of pain

acceptance and none have focused on mental defeat, despite both of these variables being associated with pain in many UK studies in the able bodied pain population. Research that includes an analysis of the impact of pain and symptoms of poor mental health over time in people with a SCI, including pain acceptance and mental defeat, could provide additional evidence supporting the idea that assessments of patients with pain should involve careful evaluation of mental state. This is to ensure that mental health problems and other psychological variables are included in treatment interventions.

7 Chapter 5 - Social Theories of Pain

Three decades ago the link between health and social relationships was established in a review associating positive social relationships with lower mortality (House, Landis, & Umberson, 1988). Since then research has widely supported its importance in maintaining good health generally, and increased survival rates (Holt-Lunstad, Smith, & Layton, 2010). It has been proposed that the way social relationships influence health may be through two processes: the main effects model and the stress-buffering model (Cohen, Gottlieb, & Underwood, 2000). The main effects model suggests that positive relationships impact on health directly through various mechanisms, such as behavioural, biological and cognitive influences. This might include conforming to health care norms, or modelling healthy behaviours. The stress-buffering model suggests an indirect route whereby social relationships moderate the effect of external stressors on health (Holt-Lunstad et al., 2010).

Where pain is concerned the influence of social relationships is thought to be equally strong (Sullivan, 2012; Craig 2009). The theories and models of pain considered so far have been intraindividual models which do not account for interpersonal factors and have been criticised as being too simplistic and lacking in explanatory power (Sullivan, 2012). In support of this, most research has focused on the biological and psychological factors involved in people's

experience of chronic pain, which misses out important social features (Craig, 2009). However, there is an interpersonal context in which pain occurs and these processes can have an influential effect on pain (Kiecolt-Glaser & Newton, 2001). An individual in pain also impacts on those around them, which can further hinder their adjustment to the pain through maladaptive interactions (Leonard, Cano & Johansen, 2006).

The Pain Overlap Theory (Eisenberger & Lieberman, 2004) takes this further by suggesting that social and physical pain share the same neural mechanisms and that these mechanisms are responsible for detecting the threat of social separation and of physical damage. For example, in one study when participants were ostracised during a ball game, the dorsal anterior cingulate cortex (dACC) and the right ventral pre-frontal cortex were activated (Eisenberger et al., 2003). Both of these areas are involved in processing the unpleasant experience of physical pain. In support of this, a physical pain suppressant will reduce activation of the dACC and also reduce hurt feelings after people are socially excluded (DeWall et al., 2010).

Further evidence of the link between social and physical pain has come from investigations into whether physical and social pain could result in the same psychological responses. When participants were either ostracised during a ball game (social pain) or were subjected to physical pain in a cold pressor test, they experienced common feelings of being excluded and ignored, and both types of pain resulted in reduced self esteem, sense of belonging and control (Riva, Wirth and Williams, 2011). Given that people who experience chronic pain often experience feelings of isolation this research demonstrates that, where pain is concerned, it is important to consider both social and physical factors and that these cannot be separated. Therefore, this chapter will focus firstly on social theories of pain, and then discuss the literature exploring the role of partner responsiveness in an individuals pain experience.

7.1 Operant Model of Pain

The operant model of pain (Fordyce, 1976) explains how the behaviours of

others towards the individual in pain can influence that individual's pain behaviours. These pain behaviours can be maintained or increased by the reinforcing or solicitous responses of friends and family members (Fordyce, 1976). In the pain literature, solicitousness refers to any response that either positively or negatively reinforces pain behaviours (Lewandowski, Morris, Draucker, & Risko, 2007). This can occur when attention is paid to the sufferer whenever they express pain and when they support the pain sufferer in avoiding undesirable activities, and in doing so fail to reward well-behaviours. The result of solicitous responses may therefore be an increase in pain behaviours and disability (Cano & Leung, 2012). In contrast, negative or punishing responses to pain, or ignoring pain and reinforcing well-behaviours, can theoretically result in reduced pain behaviour and greater activity engagement (Cano & Leung, 2012).

The operant model of pain conflicts with the idea that social support is necessarily helpful during illness, and instead, promotes the idea that its effects can be negative. There is limited research, however, that has tested this theory. Some earlier observational studies have found support for the model, for example, higher rates of spouse solicitousness have been associated with increased pain behaviours (Romano, Turner, Friedman, Jensen, & Hops, 1991; Romano et al., 1992; Paulsen & Altmaier, 1995), and have predicted greater pain-related disability in more depressed patients (Romano et al., 1995). However if the operant model is accurate, then aversive responses to pain behaviour from family members should reduce that behaviour but there is no consistent support for this. Whilst negative partner responses have been negatively associated with non-verbal pain behaviour and solicitous responses positively associated with those behaviours (Romano, Jensen, Turner, Good & Hops, 2000), this has not always been the case. In light of the conflicting evidence in the able-bodied population, how the Operant Model of Pain might apply to people with SCI, and in what way solicitous and negative responses might impact on their pain behaviours is of particular interest.

More recently, Gauthier, Thibault and Sullivan (2011) have suggested the

opposite. They explored the relationship between couples' levels of catastrophizing and pain outcomes. Additionally, they considered whether solicitous and punitive responses might act as reinforcers or punishers of the pain behaviour, helping to explain pain outcome variables. The results found that high catastrophizing pain sufferers with low catastrophizing spouses exhibited more than twice the amount of pain behaviour than couples where both partners were high catastrophizers. This suggests that a low catastrophizing spouse might inadvertently increase pain behaviour in his/her partner by ignoring or underestimating the pain they are experiencing. This causes the pain sufferer to increase their expressions of pain. As high catastrophizing is linked to increased disability the result could be worsened pain outcomes (Prkachin, Schultz,& Hughes, 2007). According to the operant model of pain, low catastrophizing should reduce pain behaviours because of the lack of reinforcement. It is important to note however, that Gauthier et al. (2011) used a self-selecting sample in a controlled laboratory setting. Their results, therefore, may not apply to patients in a pain clinic and this could explain the difference in their findings. Nonetheless, various studies support the idea that solicitousness is associated with increased pain severity and depression, but in contrast to the operant theory, so are punishing responses (Cano, Gillis, Heinz, Geisser, & Foran, 2004; Stroud, Turner, Jensen, & Cardenas, 2006).

However, lower pain-related disability has been associated with the encouragement of well behaviours (Schwartz, Jensen, & Romano, 2005), providing further support for the operant model. Overall, the evidence supports the premise that both solicitous and negative responses from spouses serve to maintain pain behaviours and disability in people with chronic pain (Pow, Stephenson, Hagedoorn, & Delongis, 2018; Cano & Leung, 2012). This suggests that despite being influential in the field of pain research, the operant model is limited in its ability to explain the interaction between an individual's expression of pain and their partner's response in the able-bodied pain population (Newton-John, 2013). Further research is now needed to determine how well partner responsiveness might predict pain outcomes in people with SCI. Partner responsiveness is discussed further later in this chapter.

7.2 Transactional Model of Health

To address some of the weaknesses of the operant conditioning model, Turk and Kerns (1985) proposed a cognitive-behavioural approach in the form of the Transactional Model of Health that applied to health and illness more generally, and more recently has been applied to pain. This model emphasises the importance not only of the family's response to pain behaviours, but also how the individual in pain appraises those responses. It suggests that the family develops stable beliefs about pain and illness, which influence the way they will appraise and respond to the challenges of chronic pain. The appraisal-coping process adopted by the family influences the way the family will adapt to the challenges, and this is further mediated by the flexibility of coping strategies and responses to stress. How the family appraises the success of their strategies determines how they will respond in future (Lewandowski et al., 2007).

The model acknowledges that because of the multidimensional nature of the pain experience, the family's response could have a positive effect on one dimension but a negative effect on another, for example, the pain sufferer's mood could be improved but disability increased by the family taking on more of the household activities. Similarly, the way a spouse copes can be either beneficial or detrimental to someone in pain, in that a solicitous response coupled with emotional support may assist a pain patient rather than reinforce pain behaviours, whereas a negative response will not necessarily be damaging if it is appraised as being driven by care and concern (Cano & Leung, 2012).

The way the intent of a partner's response is appraised, therefore, is as important in determining the consequences on pain behaviour as the response itself (Lewandowski et al., 2007). This supports earlier work demonstrating that perceived solicitousness by the individual in pain was more influential in predicting pain behaviour than self-reported solicitous responses or those that had been enacted by the partner (Flor, Kerns, & Turk, 1987; Cano, Johansen,

& Geisser, 2004). The appraisals the individual makes about their pain are also influential in the degree of distress they feel. These appraisals can be shaped by factors such as learning and mood but also by the response of significant others, which can provide support for the individual's beliefs about their pain and degree of disability (Lewandowski et al., 2007). Rather than contradicting the operant model of pain, the transactional model concurs that the response of significant others is important in the reinforcement of pain and well-behaviours. However, it also posits that the way the individual appraises their pain and the responses to it from others are equally significant.

7.3 Communal Coping Model of Pain Catastrophizing

In response to the perceived failings of cognitive models Sullivan et al. (2001) have developed a CCM of pain catastrophizing where it is suggested that pain behaviours have a strategic and communicative function. Here, interindividual processes, such as support seeking and validation, are key factors in the experience of pain-related distress. It is suggested that the expression of pain makes it more likely that others will assist and empathise, which in turn means they may expect less activity engagement from the individual in pain. This has been discussed more thoroughly in section 6.4.1 Pain Catastrophizing, above.

Much research supports the idea of pain catastrophizing having a communicative function. For example high catastrophizers use fewer coping strategies when they are with other people than when they are alone and display more pain behaviour (Sullivan, Adams & Sullivan, 2004). People are also more likely to discuss their distress with a significant other person if they are both high catastrophizers and experience more general psychological distress (Cano, Leong, Williams, May, & Lutz, 2012). This might be to maximise the likelihood of attaining their goal of gaining support. Gauthier et al's (2011) study examining the effect of high and low catastrophizing spouses on high and low catastrophizing chronic pain patients also supports the idea of the communicative function of pain and it has been demonstrated that pain behaviours can be reinforced by family members (Cano & Leong, 2012).

Holtzman and Delongis (2007) suggest that social influence mediates the effect of catastrophizing. Their research suggests that catastrophizing does not have such a negative effect on pain outcomes if there are high levels of marital satisfaction, suggesting that positive relationships can mitigate against the negative effects of catastrophic thinking. However, the duration of the pain has a moderating effect on the relationship between social support and catastrophic thinking. Solicitous responses are associated with catastrophizing at short pain durations, whereas at longer durations of pain, catastrophizing is associated with fewer solicitous responses (Cano, 2004). This suggests that whilst in the short-term catastrophic thinking may promote support from friends and family, on-going catastrophizing may result in that social support being withdrawn, possibly because of a depletion in carers' ability to continue to provide emotional support over time (Newton-John, 2013; Cano et al., 2012). This may be particularly important in SCI where pain tends to be chronic (Hagen & Rekand, 2015) and the consequences of the injury are long-term. Therefore, how carers respond over time to someone with pain and SCI is of particular interest.

Cognitive-behavioural treatments have typically not included the interpersonal aspects of pain catastrophizing. It is generally considered that for catastrophizing scores to affect clinical outcomes there needs to be a reduction in catastrophic thinking of between 25% - 30%, which is rarely achieved (Sullivan, 2012). Therefore for treatment to make a difference to pain behaviour, the interpersonal aspects of pain catastrophizing and the communication of support needs should be incorporated into pain management programmes. This may be more important than symptom reduction techniques, especially for high catastrophizers (Sullivan, 2012).

7.4 Social Communication Model of Pain

The Social Communication Model of Pain focuses on both the interpersonal and intrapersonal sources of influence for the person experiencing pain and for the caregiver or 'observer' (Craig, 2009). Where the experience of pain is concerned, intrapersonal determinants include the individual's biological

systems and also their life history (for example, their past experience of pain, culture, environment etc; Hermann, 2007; Craig, 2009). The interpersonal influences have been identified in part through various controlled studies, which demonstrated that changes in a person's social environment could change their subjective experience of pain (e.g. Craig and Coren, 1975; Craig, 2009).

Where the expression of pain is concerned, people use both verbal and non-verbal means. Non-verbal expressions of pain tend to be automatic and are often considered more credible than verbal expressions (Craig, 2009), which tend to be more controlled, as individuals can choose to be selective in what they say. However, clinicians tend to seek controlled expressions such as self-report measures because of the convenience and because it encourages interaction with patients (Craig, 2009). Intrapersonal determinants therefore, include the individual's interpersonal ability to communicate levels of pain. This should be considered in light of the fact that expressing pain does not always result in a compassionate response. Therefore whether or not someone expresses the extent of pain they are suffering may equally be as a result of situational demands as well as their subjective experience. Various studies have shown that interpersonal influences are important in the way in which pain is expressed. For example, people are more likely to show facial expressions of pain when alone (Badali, 2008) and report more pain when they are with people they perceive as being of lower status (Williams, Park, Ambrose and Clauw, 2007), demonstrating the powerful nature of social context in pain expression.

The model also considers the role of the caregiver's appraisals and assessments, recognising that this is a complex process where information is gathered from multiple sources. This might include evidence of injury and medical assessment and also factors that the caregivers themselves bring to the situation, such as personality factors and their own experience of pain. Craig (2009) suggests that the interpersonal determinants concern the types of reactions given by caregivers to the expression of pain by others. Automatic reactions tend to be intuitive and emotionally driven, whereas reflective

reactions are influenced by the caregiver's beliefs and experiences. These tend to involve cognitive reasoning processes. Reactions will vary depending on the type of pain expression; automatic expressions of pain produce automatic reactions and controlled expressions of pain produce reflective reactions (Craig, 2009). However, these reflective reactions may involve questions about the credibility of the expression of pain.

Research suggests various interpersonal influences on caregiver appraisal and assessment, for example, observers tend to take pain less seriously when there is no medical evidence for the cause of pain (De Ruddere, Goubert, Vervoort, Prkachin & Crombez, 2012). Health professionals often underestimate other people's pain (Prkachin, Solomon and Ross, 2007), whilst family and friends are more likely to overestimate the pain of a loved one, particularly if the loved one gives high pain self-reports and stops doing all tasks (Kapesser and Williams, 2008). It is possible therefore that the expressions of pain and the reactions to them are influenced by the relationship between the observer and the person in pain (Singer et al, 2006). The response of a significant other person to the individual in pain may therefore be important, and particularly so where SCI is concerned as people with SCI rate social support as indespensible to their adaptation to injury (Duggan, Wilson, DiPonio, Trumpower & Meade, 2016).

7.5 Pain and the role of the family

The role of family structures in the development and perpetuation of chronic pain supports the idea that relationships between the pain sufferer and the observer may be important (Lewandowski, 2007). There are a number of ways that one member experiencing pain can impact on the rest of the family. Role dynamics can change considerably, for example, the pain sufferer can become emotionally and physically more dependent on the family which can bring hostilities as the individual experiences a perceived loss of power. This may lead to a lack of cooperation or they may undermine the efforts of others (Cowan, Kelly, Pasero, Covington, & Lidz, 1998). There may be a role reversal and this can occur alongside added employment responsibilities for some

family members who are well (Kemler & Furnee, 2002).

Another impact can be the constriction of family life as this becomes centred on pain and illness and social activities are reduced. This in turn can lead to a sense that others outside the family don't understand the pain that is being experienced and its consequences, and can result in isolation (Soderburg, Strand, Haapala, & Lundman, 2003). Chronic pain can also have an emotional impact on family members. Feinauer and Steele (1992) have found that up to 83% of spouses experience depressive symptoms, dependent on how well the pain sufferer copes with their pain. Often spouses feel hopeless and helpless because of the uncertainty they feel about their partner's condition (Cowan et al., 1998). If the partner feels anger about the pain, it can lead to an approach-avoidance conflict, where the spouse feels compelled to help but also repelled by the anger (Lewandowski et al., 2007). All of these changes in the family can lead to a loss of intimacy between partners and families more generally (Lewandowski et al., 2007).

The role of the family in the pain experience is supported by Systems Theory (Kerns & Otis, 2003), which focuses on the dynamic nature of family relationships, and assumes that if one part of the family is dysfunctional it will lead to dysfunction in other parts of family life. This model suggests that psychological functions within the family are fulfilled in part by pain. Kerns and Otis (2003) have identified four characteristics of chronic pain families; firstly, enmeshment occurs within the family, with little or no individuation; secondly, family members become over-protective of each other; thirdly, roles and rules become inflexible and the family system becomes rigid; lastly, pain becomes a solution to interpersonal problems, where conflict within the family is not acknowledged or resolved. Pain is even perpetuated in order to avoid dealing with the conflict. Systems theory also views pain as creating a 'sick-role' identity, which allows the individual to continue their dependency on the family. The pain becomes a binding force within the family, causing enmeshment and an over-dependency on each other, and a separating force between the family and their community, causing isolation (Kerns & Otis, 2003).

Whilst operant theory, the transactional model, the CCM of catastrophizing, the social communication model and systems theory do not offer sufficient theoretical concepts about the role of social relationships in pain conditions by themselves, together they provide useful theoretical foundations that can improve understanding about the ways in which families and friends influence and are influenced by chronic pain. Where they are in agreement is the concept that the expression of pain and the response of a significant other to that pain are important in the degree to which pain adjustment occurs. How important this may be in the SCI pain population requires further attention.

7.6 The Responses of Significant Others to the Expression of Pain

Social support is a significant factor in understanding pain, and various studies have implicated it in people's experience of both chronic and acute pain. Research suggests that the unpleasant feelings associated with a painful experience, and the increased heart rate pain produces, can be reduced with social support (Che, Cash, Fitzgerald, & Fitzgibbon, 2017). This has been found when support is expressed through various means, such as social touch like hand holding and positive verbal support, implying that the effects might be greater when the support is clearly expressed in this way (Che, Cash, Chung, Fitzgerald, & Fitzgibbon, 2018). Where social touch is concerned, the positive effects occur particularly when provided by someone close to the individual (Che et al., 2018). In chronic pain conditions, even seeing images of a loved one has been associated with lower pain ratings (Shaygan, Böger, & Kröner-Herwig, 2017), supporting the suggestion that the quality of the relationship might be important where social support is concerned.

The fact that the pain experience can be influenced by the presence of social support may be related to neural activity. When looking at photographs of a romantic partner whilst being given pain, increased activity has been found in the ventromedial prefrontal cortex (VMPFC) and the posterior cingulate cortex, areas associated with safety, and decreased activity has been found in the dorsal anterior cingulate cortex (dACC) and anterior insula, areas associated

with pain processing and also with responding to the threat of pain (Eisenberger et al., 2011; Younger, Aron, Parke, Chatterjee, & Mackey, 2010). Greater perceived support was associated with reduced reported pain, greater reductions in activity in the dACC and more activity in the VMPFC (Eisenberger et al., 2011). This suggests that social support reduces the perceived threat associated with a pain experience, resulting in a lower physiological and psychological threat response (Hornstein & Eisenberger, 2017). Recently, it has also been demonstrated that the formation of fear associations is inhibited when social support is present and that this effect is maintained once a fear-inducing event is over (Hornstein & Eisenberger, 2017). The dACC is known to be associated with fear conditioning and with sustaining the fear response (Burgos-Robles, Vidal-Gonzales, & Quirk, 2009). This could explain the neural mechanisms underpinning the fear-avoidance model of pain (Vlaeyen & Linton, 2000) discussed in section 6.2 above.

Dyadic Coping Theory offers a psychological explanation of the way in which partner or spouse interactions can be impacted by stressful situations (Bodenmann, 2008). It is conceived of as a process involving three interacting factors, beginning when one partner displays stress signals, which are then perceived by the other partner. The final factor concerns the way in which this partner responds to the signals. Bodenmann (2008) proposes that dyadic coping can be common, where both partners are utilizing coping strategies for a shared stressful situation, supportive, where one partner is supporting the other through a stressful situation just being experienced by that partner, or delegated, where one partner takes over the responsibilities of the other as a way of reducing that individual's stress. This last form of dyadic coping is similar to the idea of solicitousness, where one partner reinforces pain behaviour in the other by helping them to avoid undesirable activities. Each form of dyadic coping can be either positive or negative (for example, hostile or superficial). What is key in the theory is that the response of a significant other person is influential with regards to the well-being of the other. This is particularly the case for people with chronic conditions (Revenson & DeLongis, 2010) and could therefore be applied to individuals with chronic pain and SCI.

Partner responsiveness has been identified as a significant factor in maintaining successful relationships (Reis & Gable, 2015; Debrot, Cook, Perrez,, & Horn, 2012). This is important given that a recent comprehensive review found that happy marriages have been associated with greater longevity and better physical health (Robles, Slatcher, Trombello, & McGinn, 2014) and a meta analysis of 148 studies found that the likelihood of survival increased by 50% for people with strong social relationships (Holt-Lunstad, Smith, & Layton, 2010). It has been proposed therefore, that responsiveness of the partner might be the mediator between close relationships and good health (Slatcher & Schoebi, 2017). For example, it has been associated with healthier diurnal cortisol patterns (Slatcher, Selcuk & Ong, 2015) and, whereas having an unresponsive partner predicts mortality 10 years later, this is not the case when the partner is perceived as responsive (Selcuk & Ong, 2013). Additionally, reduced immune functioning has been associated with lower perceived responsiveness (Slatcher & Selcuk, 2017). These health benefits have been found even when possible confounding variables such as physical health symptoms (Selcuk & Ong, 2013) and psychological symptoms (Slatcher et al., 2015), have been controlled for. Where pain is concerned, greater responsiveness results in an increase in endogenous opioid release (Machin & Dunbar, 2011), implying that it may be a protective factor in chronic pain conditions. This is supported by research demonstrating that perceived unresponsiveness increases the risk of developing chronic pain (Meredith, Ownsworth, & Strong, 2008) whereas greater partner responsiveness is associated with reduced pain levels (Khan et al., 2009).

In the Mutidimensional Pain Inventory partner responses have been classified as being solicitous, negative or distracting (Widerström-Noga, Duncan, Felipe-Cuervo, & Turk, 2002). Solicitous responses have been related to reduced physical activity and greater functional limitations (Hemphill, Martire, Polenick, & Parris Stephens, 2016; Raichle, Romano, & Jensen, 2011). Negative responses from spouses, whether they are expressed or perceived, are associated with worsening pain symptoms and behaviours (Burns et al., 2018). This supports earlier work showing that punishing responses are related to greater depressive symptoms, pain and relationship distress

(Newton-John & Williams, 2006; Cano, Weisberg, & Gallagher, 2000).

Additionally, increased pain throughout the day has been associated with both solicitous and negative responses (Pow, Stephenson, Hagedoorn, & Delongis, 2018). This is supported by longitudinal studies, which have found that both types of response are detrimental to the well-being of the individual in pain (Rosen et al., 2014; Song, Graham-Engeland, Mogle, & Martire, 2015). In the spinal cord injured population, distracting responses have been associated with improved pain control and mental health (Henwood & Ellis, 2004; Widerström-Noga, Felix, Cruz-Almeida, & Turk, 2007), although like solicitousness, a distracting response from another person has also been associated with higher reported pain severity, whilst negative responses have been associated with higher catastrophizing (Taylor et al., 2012). Distracting and negative partner responses have also been associated with higher depressive symptoms (Stroud, Turner, Jensen, & Cardenas, 2006). Clarifying which types of responses are beneficial and which may have a negative impact for people with SCI is important if social support is to assist with adaptation to injury.

Although much of the evidence points to the negative effects of solicitousness, there are inconsistencies in the literature. One longitudinal study did not find a significant relationship between solicitous responses and poorer physical functioning, although there was a trend in that direction (Wilson, Martire, & Sliwinski, 2017). The authors suggest that this might reflect the fact that partners may not have been consistently solicitous in their response, and instead might have adjusted their way of responding to the patients varying needs (Wilson et al., 2017). Interpersonal judgements might also explain some of the differences found in studies. They are particularly important as the accurate perception of the degree of pain being suffered is necessary to giving effective care. Underestimations of pain might result in a negative response but may be caused by individuals with chronic pain giving fewer pain signals than those with acute pain or that chronic pain sufferers may feel inhibited because of the possible stigma associated with it or because of a desire to be seen to be coping (Goubert et al., 2005). Alternatively observers may

underestimate the pain in others as a way of coping with their own distress (Prkachin, Solomon, Hwang, & Mercer, 2001). Overestimations of pain may also be problematic as it may encourage the pain sufferer to re-evaluate their pain as being worse than it is. The overestimation of pain may lead the observer to do more for the person than is necessary, leading to reduced functioning and greater disability (Goubert et al., 2005).

The idea that too much support may have negative consequences has been supported in more recent studies. Although individuals in pain have rated social support from friends and family as being the most valued type of social interaction they receive (Kostova, Caiatta-Zufferey, & Schulz, 2014), over-support in the form of solicitousness, can inhibit acceptance and adaptation to a pain condition (Kostova et al., 2014). This relationship exists the other way around, as pain acceptance is associated with fewer negative and fewer solicitous responses from a spouse (McCracken, 2005). An associated concept, that of mindfulness, has also been associated with fewer negative spousal responses and greater social support when practiced by the individual in pain (Williams & Cano, 2014). It is possible that such solicitous responding to an individual's pain may lead to a vicious cycle. Reverse causation analyses have found that not only does solicitousness result in increased pain, but that the increased pain produces greater solicitousness (Pow et al., 2018), demonstrating how social factors might be involved in the transition from acute to chronic pain.

The importance of social support has been recognized in the spinal cord injured population with poor social relationships predicting mental health problems and being negatively associated more generally with wellbeing (Zurcher, et al., 2019; Tough, Siegrist, & Fekete, 2017). This is the case where the size of the network, the quality of the relationships and the frequency of contact are concerned (Helgeson, 2003). In contrast, a low risk of psychological disorders is associated with high social support (Craig et al., 2015). As stated previously, pain and mental health problem comorbidity is common in both the able-bodied and spinal cord injured populations (Carleton et al., 2018; Tran, Dorstyn & Burke, 2016).

People with SCI recognise the value of social support, stating that the support of friends and family, as well as support from health professionals, has been indispensable in their ability to adapt to the challenges associated with the injury (Duggan, et al., 2016). A recent qualitative study identified three types of support perceived as being particularly valuable: help from friends and family to engage in valued activities, motivation and encouragement to engage in activities of daily living and look positively on the future, and support in taking back on former roles and responsibilities (Duggan et al., 2016). This suggests that the kind of support most valued is the kind that encourages resilience and adaptation, rather than support that removes responsibility from the individual. It is possible therefore, that solicitous responses that enable the individual to engage in activities and renew responsibilities might be beneficial to someone with SCI.

The value of enabling support is reflected in the literature focusing on social participation, which is an important aspect of adjustment to SCI following discharge from rehabilitation services (Craig, Nicholson Perry, Guest, Tran, & Middleton, 2015). Social participation involves being self-managed, and being able to choose to participate in activities in the community (Moss-Morris, 2013). In the able-bodied population positive social interactions have been related to reduced pain and greater resilience in the presence of pain (Zautra, Johnson, & Davis, 2005). However, many factors associated with SCI, including pain (Donnelly & Eng, 2005) and psychological comorbidity (Craig, Guest, Tran, Nicholson Perry, & Middleton, 2017), make social participation challenging, and it has been reported that up to 80% of people experience limitations to the extent to which they are able to engage in social activities (Carpenter, Forwell, Jongbloed & Backman, 2007). This is important because social participation predicts better perceived quality of life (Erosa, Berry, Elliott, Underhill, & Fine, 2014), and has been negatively associated with unemployment (Craig et al., 2015). However, certain factors can aid reintegration into the community, such as strong social support, a sense of personal control and self-efficacy predict better social participation (Craig et al., 2015; Song, 2005). This implies that a consideration of social networks

and developing a sense of autonomy should be included as rehabilitation goals.

It has been suggested that social support might not be a unitary construct as different types of social support have been associated with different outcomes in the spinal cord injured population (van Leeuwen et al., 2010). For example, a positive association between life satisfaction and everyday social support has been found, but a negative association between life satisfaction and support in problem situations exists (van Leeuwen et al., 2010). Support in problem situations might reflect more problem-oriented support, which has been negatively related to life satisfaction in earlier research (Helgeson, 2003). It is possible that this type of support highlights the individual's disability (Helgeson, 2003) or tries to take over responsibilities and in this way could be closely related to solicitousness.

Solicitousness can impact on pain-related outcomes more broadly than just pain intensity, also having a negative association with the severity of insomnia in people with chronic pain (Jensen, Woodhouse, Butler, Borchgrevink, & Stiles, 2018). This could exacerbate what is already a problem for people with SCI (Fogelberg, Hughes, Vitiello, Hoffman, & Amtmann, 2016). Additionally, solicitous responses from a significant other have been associated with increased visits to physicians, possibly because the pain behaviour is reinforced, resulting in a perception of needing greater professional support (Vriezekolk, Peters, van den Ende, & Geenen, 2019). Negative responses also impact on pain more widely than pain intensity, and have been correlated with greater interference in activity engagement (Stroud, Turner, Jensen, & Cardenas, 2006). In this same study, no association was found between activity interference and partner solicitousness (Stroud, et al., 2006), which contrasts with other research results in the able-bodied populations (Hemphill, Martire, Polenick, & Parris Stephens, 2016). It is possible that negative responses are a more powerful negative influence in the adaptation to pain and SCI and that solicitous responses are necessary to enable people with SCI to engage in the activities that interest them.

The contradicting findings regarding partner responses to pain might reflect the possibility that people with SCI and pain are not a homogenous group. It is also possible that the influence of social support may be different in patients with chronic pain and SCI than in other chronic pain groups. Three subgroups have been identified in the wider chronic pain population and been confirmed across various pain diagnostic groups: a dysfunctional group characterized by high pain severity, pain interference and affective distress, and low activity levels and sense of control; an adaptive copers group with lower pain, interference and distress but higher activity levels and perceived control; and an interpersonally distressed group with high pain levels and low emotional, instrumental and social support (Turk & Rudy, 1988).

Widerström-Noga, Felix, Cruz-Almeida, and Turk, (2007) were interested in whether people with SCI and pain would map on to these same clusters. They found that in the spinal cord injured chronic pain population the dysfunctional and adaptive copers groups were apparent and had similar characteristics to those found in the able-bodied populations. However, in contrast to the earlier study, the third group was identified as an interpersonally supported group. This group was characterized by high levels of pain-specific support in the form of distracting and solicitous responses and general social support from significant others. Although individuals in this group reported high pain severity they had lower interference from pain, lower affective distress, and higher activity levels and perceived control than the dysfunctional group (Widerström-Noga et al., 2007). Both the dysfunctional and the interpersonally supported groups had higher levels of positive support than the adaptive copers, and had higher pain levels, suggesting that support of this nature is offered in response to severe pain (Widerström-Noga et al., 2007). There were differences between these two subgroups however, with more positive pain-related support being found in the interpersonally supported group and more negative pain-related responses being found in the dysfunctional group. This supports the view that negative responses are associated with greater functional interference and distress. However, given that both of these groups reported higher pain levels and more frequent positive social support in the form of solicitous responses than the adaptive copers, it also concurs with previous

research linking solicitousness and negative responses with pain intensity (Pow et al., 2018). The differences seen in the way the dysfunctional group and the interpersonally supported group adapt to these high pain levels might be explained by differences in the frequency of negative responses received and in the other types of positive social support, such as distracting responses, leading to better outcomes in the interpersonally supported group (Widerström-Noga et al., 2007).

This study suggests that, although some similarities are apparent between spinal cord injured and other pain groups, there are also differences. Whereas in the able-bodied chronic pain population it is the presence of negative pain support and the lack of positive pain-related support that is more influential in adaptation to pain, it would appear that for people with SCI, at least in the interpersonally supported group, it is the presence of positive support that makes a difference. This might reflect the additional problems experienced in this group from other consequences of their injury, which require more support from significant others. Therefore, solicitousness could be beneficial to people with SCI and pain in a way that it is not for the able-bodied pain population. Given that the response of others to people in pain with SCI has not received the same level of attention as many psychological factors, it is important to include this in biopsychosocial research.

Whilst the way in which a partner responds to an individual in pain is clearly influential, there have been criticisms of the limited range of responses studied. The Multidimentional Pain Inventory's 'significant other response scale' (Widerström-Noga, Duncan, Felipe-Cuervo, & Turk, 2002), used by many researchers, categorises spouse responses into three areas; solicitous, punishing or negative, and distracting. Some problems have been identified with this in that it suggests that responses are consistently either punishing, distracting or solicitious which assumes that spouses are consistent in the way they respond to their partner in pain (Newton-John, 2002). It is possible that spouses are more likely to use a variety of responses depending on the situation. For example, in a qualitative study by Newton-John and Williams (2000) spouse responses were categorised into 12 different categories,

included in which were four different categories of solicitousness. This suggests that the concept of solicitousness has greater complexity than can be explained in a single definition.

More recently the use of solicitousness as a measure of social support has been criticised as lacking depth and breadth and often being analysed without consideration of the context in which it is provided (Bernardes, Forgeron, Fournier, & Reszel, 2017). However, there is value in exploring more general categories of response and the Multidimensional Pain Inventory examines partner responses in a much broader context, also considering a variety of pain-related outcomes and activity engagement (Widerström-Noga, Duncan, Felipe-Cuervo, & Turk, 2002). Additionally Bernardes et al. (2017) have called for more studies to explore the mediation pathways of social support, and to use longitudinal designs in order to improve understanding of what is an important part of the pain experience. This may be more important than over-complicating the construct of partner responsiveness.

7.7 Conclusion

Understanding the social context of pain is equally as important as understanding the biological and psychological contexts, however, in the SCI population there have been fewer studies carried out in this area. Social support in general is associated with psychological well-being (Zurcher, et al., 2019). More specifically, the way a partner responds to an individual's pain can be highly influential, impacting on pain severity (Burns et al., 2018), pain-related disability (Slatcher & Schoebi, 2017), pain-related distress (Taylor et al., 2012), activity engagement and adaptation to the pain (Stroud et al., 2006). This has been found in the SCI pain population as well as the able bodied population in the UK and more widely across Europe, North America and Australia. However, the way in which partner responsiveness interacts with other pain variables to affect pain-related outcomes has been studied less, and what might mediate the relationship between responses and outcomes requires further analysis. Additionally, it remains unclear whether

solicitous responses to the expression of pain are beneficial or detrimental to the wellbeing of people with SCI and pain. Therefore, the way a significant other person in the patient's life responds to their pain will be explored.The relationship between patients and healthcare professionals is not included in this thesis.

8 Chapter 6 - Study Rationale

For people with a SCI, pain remains one of the most debilitating sequelae of the condition (Tran, Dorstyn, & Burke, 2016), affecting between 61% and 76% of people (Finnerup et al., 2016). Pain can be either nociceptive or neuropathic, with many people experiencing both (Hagen & Rekind, 2015). Neuropathic pain is particularly difficult to treat (Teasell, et al., 2010), which is problematic because of the high levels of distress and disability associated with it (Gruener, Zeilig, Laufer, Blumen & Defrin, 2018). Additionally, it is known that adaptation to SCI is hindered by the presence of both types of pain (Craig, Guest, Tran, Nicholson Perry & Middleton, 2017), but that pain management programmes that have been successful in the able-bodied chronic pain population, have not been so effective for people with SCI (Perry, Nicholas & Middleton, 2010).

Various biopsychosocial variables have been implicated in the experience of pain, but these have rarely been examined together. Whilst the association between pain and depression, anxiety and pain catastrophizing has been well documented in the SCI pain population, pain acceptance has received less attention and mental defeat has not been studied at all. It is important therefore to enhance understanding about whether the latter two psychological variables are influential in SCI pain, and how all these variables might interact

to impact pain outcomes. Alongside these factors, responses from a significant other to the expression of pain has been associated with various pain outcomes in the SCI pain population. However, this has not been examined in combination with biopsychological factors. Additionally, whilst a relationship between cortisol and SCI has been established, cortisol and the stress response has not been considered more specifically in relation to pain, or in combination with these other factors in people with SCI. This represents a significant gap in the literature. The over riding research question that this study seeks to answer therefore is: **in what way do biopsychosocial variables interact to impact pain-related outcomes, and which factors have the greatest effects?**

After suffering a SCI people spend many months in hospital, receiving extensive rehabilitation treatment. Few studies focusing on SCI and pain have been longitudinal and even fewer have compared in-patients and out-patient samples. Those that have report conflicting results (Kennedy & Rogers, 2000), indicating that further research needs to explore whether any differences between these two groups exist. **The research question is: do differences exist between in-patient groups and out-patients on biopsychosocial variables?** Given that people who have been discharged from hospital might have had more time to adjust to their injury, it was expected that differences may be found. Which direction this might take was less clear, and therefore this part of the study was exploratory. In-patients were asked to participate on three occasions over a nine month period (see section 9.3.1.2 In-Patient Study). The first and third in-patient time points were used in this part of the analysis because it was likely that by time three most participants would be recently discharged. It would be possible to see whether any differences that exist between in-patients at time one and out-patients resolve or increase once people were no longer in hospital. In-patients at time two are more likely to be mixed with regards to whether they have been discharged or not, making the comparison with out-patients less clear. In-patients at time three may still show differences with out-patients because the time since discharge will be

greater for the out-patient group. The first hypothesis, therefore, is that differences would be found in all variables between the in-patient and out-patient samples, but this remains a two-tailed hypothesis.

Research into the effects of negative psychological variables and pain have not always found an association between the variables analysed and pain intensity (Kim, Williams, Hassett, & Kratz, 2019; Finnerup et al., 2016), although sometimes this relationship has been established (Meints et al., 2019). For example, mental defeat (Hezeldene-Baker, Salkovskis, Osborn, & Gauntlett-Gilbert, 2018) pain catastrophizing (Meints et al., 2019), perceived stress (Fischer et al., 2016), depression and anxiety (Tran, Dorstyn, & Burke, 2016) have all been positively associated with pain intensity in some studies but also with pain interference, distress and increased disability. This suggests that the pain outcomes included in research need to be broader than simply pain intensity, and include pain interference and pain-related distress. Depression and pain catastrophizing have been quite widely researched in people with SCI, with studies generally showing that these factors interfere with adaptation to injury (Kim et al., 2019; Battalio, Glette, Alschuler, & Jensen, 2018). Anxiety and perceived stress have had less of a focus, despite them both contributing to greater difficulties in SCI (Tran et al., 2016). No studies were found that included mental defeat and SCI, even though in the able bodied population it has been associated with increased pain intensity and interference (Hezeldene-Baker et al., 2018), and an increased risk of suicidal ideation when pain and disability were combined (Racine, 2018).

Of additional interest is how appraisal of injury might combine with other psychological variables to impact on pain outcomes as this has not been studied before. Negative appraisals (catastrophic negativity) have been found to predict psychological distress (Kennedy, Kilvert, & Hasson, 2016) and functional outcomes (Kennedy et al., 2010) following SCI, but appraisal has only been looked at either in pain conditions or in SCI, but not in both conditions combined. How these negative psychological factors combine to impact on pain outcomes is not clear as studies have typically not included a wide range of possible psychological predictors in the model. **The research**

question therefore is: do negative psychological variables predict pain intensity, life interference from pain, and pain-related distress in people with a SCI? To answer this, the study grouped the negative psychological variables of catastrophic negativity (as an appraisal of injury), pain catastrophizing, perceived stress, mental defeat, depression, and anxiety and hypothesised (hypothesis 2) that they would predict an increase in all pain-related outcomes. Additionally, because research suggests that the different sub scales of pain catastrophizing might affect pain outcomes differently (Craner, Gilliam and Sperry, 2016), this study looked at their predictive power in combination and individually.

Where positive psychological factors are concerned pain acceptance has been widely researched in the general pain literature but less so in SCI. Pain acceptance has been related to reduced pain intensity and physical disability in the wider population (Craner, Sperry, Koball, Morrison, & Gilliam, 2017), and spinal cord pain studies have identified positive pain-related outcomes associated with it (Kim et al., 2019). As with pain catastrophizing, the sub scales of pain acceptance, pain willingness and activity engagement, have been found to affect pain outcomes in different ways (Kratz, Hirsh, Ehde & Jensen, 2013), justifying their inclusion as separate variables rather than examining acceptance as a unitary factor. In addition to acceptance, resilience as a form of injury appraisal has been included as it has been shown to facilitate adjustment to injury (Duggan, Wilson, DiPonio, Trumpeter, & Meade, 2016) but has not been looked at in pain and SCI combined. **The research question is: do positive psychological variables predict pain intensity, life interference from pain, and pain-related distress in people with a SCI?** It is hypothesised (hypothesis 3) that these positive psychological variables will predict a reduction in pain outcomes.

The relationship between social support and psychological and physiological well-being has been widely established (Zurcher et al., 2019). However, there is conflicting evidence regarding the impact of partner responses to pain. Some studies have found that solicitousness is negatively associated with pain-related outcomes (Jensen, Woodhouse, Butler, Borchgrevink, & Stiles,

2018) whereas other studies have not found an association between these variables (Stroud, Turner, Jensen, & Cardenas, 2006). Similarly, research suggests that a distracting response from a significant other results either in better pain control (Henwood & Ellis, 2004) or contrastingly, greater pain severity (Taylor et al., 2012). Studies agree on the negative impact of punishing or negative responses (Stroud et al., 2006). These conflicting findings need clarifying in the spinal cord injured population to determine whether a particular type of response may be predictive of certain pain-related outcomes. **The research question therefore, is: does the way a significant other person responds to someone in pain (solicitous, distracting or negative) affect pain-related outcomes of pain intensity, life interference and pain-related distress?** It is hypothesised (hypothesis 4) that each type of response will predict pain outcomes, although the direction of the effect is not speculated.

Cortisol production has been associated with the experience of pain with and without the presence of tissue damage (de Quervain, Schwabe, Roozendaal, 2017). It is also associated with various psychological and social variables. For example, both increases and decreases in cortisol production have been linked to anxiety and depression, possibly reflecting the acute and chronic stages respectively of these conditions (Vreshek-Schallhorn,2013; Steudte-Schmiedgen, et al., 2017). Unsurprisingly, given that cortisol production is part of the stress response, it is also associated with perceived stress (Fries, Hesse, Hellhammer & Hellhammer, 2005). There has been less research looking at links between cortisol concentration levels and other psychological variables, however in the social literature, where partner responsiveness is concerned, a steeper cortisol diurnal slope has been associated with positive responses (Slatcher, Selcuk, & Ong, 2015), and a flatter pattern linked to negative affect (Selcuk, Gunaydin, Ong, & Almeida, 2016). Given that both hypocortisolism and hypercortisolism are associated with immune system dysfunction it is particularly important to clarify how cortisol is related to psychosocial variables, as poor immune functioning has potentially serious consequences for people with SCI who are at greater risk of infection from things such as pressure sores (Allison & Ditor, 2015). **The research question**

is: do cortisol concentration levels predict pain intensity, life interference and pain-related distress, and is cortisol concentration associated with negative psychological variables, positive psychological variables, others responses and pain outcome variables? Given the literature associating pain and cortisol, it is hypothesised (hypothesis 5) that higher cortisol concentration will predict increased pain-related outcomes. Additionally, it is predicted that cortisol concentration will be associated with both positive and negative psychological factors and with the responsiveness of significant others to those in pain, but the direction of the association is not speculated (hypothesis 6).

The majority of research into SCI has been cross-sectional. However, where longitudinal studies have been carried out it has been suggested that a substantial minority of individuals go on to experience increased psychological distress after transitioning back to the community suggesting that their symptoms maintain or worsen over time (Craig et al., 2015). However, research has also found that the majority of people adjust well to their injury and experience psychosocial improvement as they adapt to the consequences of the injury (Kennedy & Rogers, 2000). **The research question therefore is: do biopsychosocial factors improve over time as people adapt to their injury?** It was hypothesised (hypothesis 7) that, for the in-patient group, biopsychosocial outcomes would collectively improve and stabilise over a nine-month period as people adapt to their SCI, but have not had long enough in the community for the challenges of daily living to increase. Additionally, across both groups it was predicted that there would be an association between time since injury and each variable (hypothesis 8) but the direction of the relationship is not hypothesised.

To summarise, much research has been carried out into pain conditions in SCI but, although it is widely recognised that pain is a biopsychosocial condition, most research looks at one or two factors rather than including all elements of the model. The aim of this study is to explore how psychological factors, social factors and the biological measure of cortisol interact with each other to affect the experience of pain in people with a SCI. Also of interest is whether the

influence of these factors changes over time. Depending on the results of the initial analyses, further follow-up exploratory analysis may be undertaken. To summarise, the following research questions and hypotheses are made:

Overarching research question: In what way do biopsychosocial variables interact to impact pain-related outcomes, and which factors have the greatest effects?

Research question one: Do differences exist between in-patient groups and out-patients on biopsychosocial variables?

- Hypothesis 1a - There will be a significant difference in scores on all measures between in-patients at time one and out-patients.
- Hypothesis 1b - There will be a significant difference in scores on all measures between in-patients at time three and out-patients.

Research question 2: Do negative psychological variables predict pain intensity, life interference from pain, and pain-related distress in people with a SCI?

- Hypothesis 2a - Negative psychological characteristics will predict increased pain intensity scores.
- Hypothesis 2b - Negative psychological characteristics will predict increased life interference from pain.
- Hypothesis 2c - Negative psychological characteristics will predict increased levels of pain-related distress.

Research question 3: Do positive psychological variables predict pain intensity, life interference from pain, and pain-related distress in people with a SCI?

- Hypothesis 3a - Positive psychological characteristics will predict a reduction in pain intensity scores.
- Hypothesis 3b - Positive psychological characteristics will predict a reduction in the extent to which pain interferes with everyday life
- Hypothesis 3c - Positive psychological characteristics will predict a

reduction in levels of pain-related distress.

Research question 4: Does the way a significant other person responds to someone in pain (solicitous, distracting or negative) affect pain-related outcomes of pain intensity, life interference and pain-related distress?

- Hypothesis 4a - The way a significant other person responds to the individual in pain will predict pain intensity scores.
- Hypothesis 4b - The way a significant other person responds to the individual in pain will predict the extent of life interference from pain.
- Hypothesis 4c - The way a significant other person responds to the individual in pain will predict levels of pain-related distress.

Research question 5: In what way is cortisol concentration associated with pain outcomes and the biopsychosocial variables?

- **Research question 5a**: Do cortisol concentration levels predict pain intensity, life interference and pain-related distress?
    - Hypothesis 5ai - Cortisol concentration levels will predict an increase in pain intensity scores
    - Hypothesis 5aii - Cortisol concentration levels will predict an increase in the extent of life interference from pain.
    - Hypothesis 5aiii - Cortisol concentration levels will predict an increase in levels of pain-related distress.

- **Research question 5b**: Is cortisol concentration associated with negative psychological variables, positive psychological variables, others responses and pain outcome variables?
    - Hypothesis 5bi - There will be a relationship between cortisol concentration levels and negative psychological variables.
    - Hypothesis 5bii - There will be a relationship between cortisol concentration levels and positive psychological variables.
    - Hypothesis 5biii - There will be a relationship between cortisol concentration levels and others' responses.

- Hypothesis 5biv - There will be a relationship between cortisol concentration levels and pain outcome variables.

Research question 6: Do biopsychosocial factors improve over time as people adapt to their injury?

- Hypothesis 6a - As in-patients adapt to their SCI, their biopsychosocial outcomes will collectively improve and stabilise.
- Hypothesis 6b - There will be a relationship between time since injury and each variable.

To conclude, the experience of pain involves biological factors in terms cortisol secretion, emotional responses, pain beliefs, fear-avoidance strategies, problem solving attempts and social influences to name just a selection. These need to be examined in the spinal cord injured population in a cohesive way if treatment interventions are to improve outcomes in pain patients and to reduce the likelihood of acute pain developing into chronic pain.

9 Chapter 7 - Method

9.1 Participants

Participants were sourced through the National Spinal Injuries Centre (NSIC) at Stoke Mandeville, Buckinghamshire and the SIA in Milton Keynes. A power calculation was carried out to determine appropriate sample sizes for the different types of analyses used (see section 9.5 Statistical Analysis).

9.1.1 Out-Patient Sample

In the cross-sectional study, out-patients with chronic pain were invited to join the study if they had been discharged from hospital for a minimum of two years. 322 people were identified through the NSIC as meeting the recruitment criteria. 62 (19%) of these returned a consent form. Individuals were also approached at the out-patients clinic at the NSIC but no further participants were generated by this method as they either did not meet the recruitment criteria or had already been contacted as in-patients or out-patients. One further person was recruited through the SIA. From all those who had consented to take part in the research a total of 47 (75%) participants (17 (36.2%) females and 30 (63.8%) males) completed the questionnaires and provided saliva samples, with ages ranging from 24 to 88 (M = 56.94, SD =

14.87). The demographic and clinical data of the out-patient sample is shown in Table 3.

9.1.2 **In-Patient Sample**

For the in-patient participants, 162 in-patients in the three rehabilitation wards of the NSIC who met the inclusion criteria listed below were invited to join the study. 60 (37%) of these agreed to participate, 17 (28.3%) females and 43 (71.7%) males with ages ranging from 18 to 82 (*M* = 49.62, SD = 15.87). The demographic and clinical data of the in-patient sample is shown in Table 3. In-patient participants were asked to participate in the study at three time points over a nine-month period. Of the 60 participants who completed the study at the first time point, 29 (48%) continued to participate at Time two (T2) and/or Time three (T3). Table 2 below shows the number of participants participating at each stage of the longitudinal study, and the numbers included in the study after missing data had been dealt with using imputation methods (see section 9.5 Statistical Analysis). This is shown in greater detail in Figure 19, section 9.3.1.2.

Table 2. Numbers of in-patients participating at each time point of the longitudinal study.

Numbers Completing Time 1	Numbers Completing Time 2	Numbers Completing Time 3	Numbers Included in Study After Imputation
60	23	21	29

9.1.3 **Inclusion Criteria**

Individuals were invited to join the study if they were 18 years or over, they had been diagnosed with a SCI which had resulted in complete or incomplete tetraplegia or paraplegia and they had reported experiencing pain on the Adult Needs Assessment Checklist at the NSIC (in-patients), or on the Leeds Assessment of Neuropathic Symptoms and Signs (LANSS; Bennett, Smith, Torrance & Potter, 2005) questionnaire (out-patients).

9.1.4 **Exclusion Criteria**

Individuals were excluded if they were not experiencing pain, did not speak English, were illiterate, had a significant head injury or communication disorder that would impair their ability to complete questionnaires or who were considered by ward staff to be too physically unwell to participate (following Kennedy, Evans and Sandhu,2009).

Table 3. Demographic and clinical data of in-patient and out-patient participants.

Variable	In-Patients	Out-Patients
Total Number	60	47
Sex - *n* (%)		
Female	17 (28.3%)	17 (36.2%)
Male	43 (71.7%)	30 (63.8%)
Marital Status - *n* (%)		
Married	27 (45%)	24 (51.1%)
Divorced	6 (10%)	8 (17%)
Separated	1 (1.7%)	0
Cohabiting	3 (5%)	2 (4.3%)
Single	18 (30%)	11 (23.4%)
Widowed	5 (8.3%)	2 (4.3%)
Education - *n* (%)		
Postgraduate	4 (6.7%)	5 (10.9%)
Degree	11 (18.3%)	9 (19.6%)
A Level or equivalent	19 (31.7%)	12 (26.1%)
GCSE or equivalent	17 (28.3%)	14 (30.4%)
Other	4 (6.7%)	3 (6.5%)
No formal qualifications	5 (8.3%)	3 (6.5%)
Not stated		1

Variable	In-Patients	Out-Patients
Ethnicity - *n* (%)		
White British	52 (86.7%)	35 (74.5%)
White European	2 (3.4%)	2 (4.2%)
White other	2 (3.3%)	2 (4.3%)
Indian	0	2 (4.3%)
Pakistani	1 (1.7%)	0
Bangladeshi	1 (1.7%)	0
Chinese	0	1 (2.1%)
Other Asian	0	1 (2.1%)
Black Caribbean	0	1 (2.1%)
Black African	1 (1.7%)	2 (4.3%)
Black other	1 (1.7%)	0
Other ethnicity	0	1 (2.1%)
Time since SCI - Mean months (SD)	9.41 (26.21)	69.25 (89.10)
Level of Injury - *n* (%)		
C1-C8	32 (53.3%)	23 (48.9%)
T1-T12	20 (33.4%)	19 (40.4%)
L1-L5	8 (13.3%)	3 (6.4%)
S1-S5	0	0
Not stated	0	2 (4.3%)
Injury Status - *n* (%)		
Incomplete tetraplegia	20 (33.3%)	14 (29.8%)
Complete tetraplegia	4 (6.7%)	3 (6.4%)
Incomplete paraplegia	31 (51.7%)	10 (21.3%)
Complete paraplegia	4 (6.7%)	14 (29.8%)
Not stated	1 (1.6%)	6 (12.7%)

Variable	In-Patients	Out-Patients
Cause of SCI - *n* (%)		
Road traffic accident	11 (18.3%)	9 (19.2%)
Fall	15 (25%)	15 (31.9%)
Sporting injury	8 (13.3%)	7 (14.9%)
Non-traumatic condition	9 (15%)	4 (8.5%)
Other	16 (26.7%)	12 (25.5%)
Not stated	1 (1.7%)	0
ASIA rating scale - *n* (%)		
ASIA A	6 (10%)	16 (34%)
ASIA B	11 (18.4%)	5 (10.6%)
ASIA C	14 (23.3%)	3 (6.4%)
ASIA D	15 (25%)	21 (44.7%)
Not stated	14 (23.3%)	2 (4.3%)

9.2 Materials

Two types of questionnaire were used for this study and are described in detail below; i) two standard validated measures of pain; ii) six standard validated questionnaires to assess the psychological factors of perceived stress, pain catastrophising, self-appraisals of disability, mental defeat, acceptance of pain and two aspects of mental health; anxiety and depression. The questionnaires have all been widely used in other research (see below) and this provides the opportunity to compare the behaviour of the data between studies. Which questionnaires were used at which timepoints can be found in Table 4 below.

9.2.1 Questionnaires

9.2.1.1 Two pain measures:

1. **Leeds Assessment of Neuropathic Symptoms and Signs (S-LANSS)**

The S-LANSS (Bennett, Smith, Torrance & Potter, 2005) is a self-administered 9-item questionnaire, which can be used for assessing the location and type of

pain a person may be experiencing (nociceptive or neuropathic) and its severity. In the first section of the questionnaire participants are asked to draw on a diagram of a human body where they are experiencing pain and to indicate the degree of that pain in the previous week on a numerical rating scale where 0 = no pain and 10 = pain as severe as it could be. Numerical ratings scales have been recommended for use as an outcome measure for pain intensity following SCI (Bryce et al., 2007). In the second section seven questions ask for fixed response answers (yes/no). Negative responses have a score of zero and positive responses have a weighting of between 1 and 5, depending on the question. A score of 12 or more is indicative of neuropathic pain. It has been validated in a community chronic pain sample and has been shown to have good internal consistency (α = 0.76 - 0.87, Bennett et al., 2005; Weingarten et al., 2007). It has also been recommended for discriminating between nociceptive and neuropathic pain following SCI (Bryce et al., 2007).

2. **Multidimensional Pain Inventory - SCI (MPI-SCI)**

Adapted specifically for the spinal cord injured population from the West Haven-Yale Multidimensional Pain Inventory (Kerns, Turk, & Rudy, 1985), the MPI-SCI (Widerström-Noga, Duncan, Felipe-Cuervo, & Turk, 2002) is a 56-item self-report questionnaire in three sections, which assesses the impact of pain on daily living. Section A consists of 20 questions, using a 7-point likert scale, focusing on how pain affects the individual's life, for example, "How much has your pain changed your ability to do household chores?", with the end points 0 = no change and 6 = extreme change. This section has five sub-scales pertaining to pain outcomes: Life Interference, Support, Life Control, Pain Severity and Affective Distress. Section B asks twelve questions regarding the frequency with which a 'significant other' person in the individual's life responds to their pain in a particular way, for example, "Tries to involve me in some activity". Answers fall on a 7-point likert scale with the end points 0 = never and 6 = very often. This section has three sub scales: distracting responses, negative responses, and solicitous responses. Section C also uses a 7-point likert scale and has 18 questions asking how often the individual engages in particular activities (0 = never, 6 = very often) and the degree to which pain has reduced that participation (0 = not at all, 6 =

extremely). For the in-patient sample only section B was used whilst they were still in hospital as the other two sections have questions that were not relevant to them, for example, 'How often do you go grocery shopping?'. This section has been widely used independently of the rest of the questionnaire in research looking at the social factors of chronic pain, as highlighted by Goossens, Dousse, Ventura and Fattal, (2009) in their review examining whether social and environmental factors could predict pain or its chronicity in people with SCI. The MPI-SCI has been found to have high validity and reliability in the measurement of chronic pain in people with a SCI and good internal consistency (α = 0.62 - 0.94, Widerström-Noga, Cruz-Almeida, Martinez-Arizala & Turk, 2006). However, for some of the analyses sub-scales of Section A were used to measure affective, sensory and functional aspects of pain, which means these measures of reliability and validity are tentative. The results section clearly states which scales were used in each type of analysis.

9.2.1.2 Six psychological measures:

1. **Perceived Stress Scale (PSS-10)**

The PSS-10 (Cohen, Kamarck & Mermelstein, 1983) is a 10-item measure designed to assess the extent to which situations in an individual's life are perceived as being stressful. It also asks direct questions about the current level of stress being experienced. Participants rate how often they have thought or felt a certain way during the previous month using a 5-point Likert scale, for example, "In the last month, how often have you been upset because of something that happened unexpectedly?". This scale uses the end points 0 = never and 4 = very often and the total score ranges from 0 to 40. A higher score suggests a greater level of perceived stress. The PSS-10 has been found to have strong internal consistency, validity and reliability (Cohen, 1988; Roberti, Harrington & Storch, 2006). It has been widely used in research involving people with a SCI, positively correlating with depression and stressful life events and negatively correlating with quality of life suggesting good internal validity for this population (Rintala, Robinson-Whelen & Matamoros, 2005; Ginis et al., 2003; Gerhart, Weitzenkamp, Kennedy, Glass & Charlifue,

1999).

2. **Pain Catastrophising Scale (PCS)**

The PCS (Sullivan, Bishop & Pivik, 1995) is a 13-item scale which measures the degree to which people experience catastrophic thinking with regards to their pain using three subscales; rumination, magnification and helplessness. Participants rate how frequently they experience catastrophic thoughts such as, “I become afraid the pain may get worse”, on a 5-point Likert scale with the end points 0 = not at all and 4 = all the time. The total score ranges from 0 to 52, with higher scores suggestive of more frequent catastrophic thinking. The individual subscale scores range from 0 to 16 for rumination, 0 to 12 for magnification and 0 to 24 for helplessness. As with the total score, higher scores reflect higher levels of thinking of the type reflected by the subscale. The PCS has been found to have good internal consistency ($\alpha = 0.92$) reliability and internal validity in an adult sample of chronic pain patients (Osman, Barrios, Gutierrez, Kopper, Merrifield & Grittmann, 2000). Although it has not been specifically validated for use with people with SCI, it has been used to assess catastrophising in a sample of adults with neuropathic pain (Sullivan, Lynch and Clark, 2005) and with phantom limb pain (Vase et al., 2011).

3. **Appraisals of Disability: Primary and Secondary Scale (ADAPSS)**

Designed to assess the way people with a SCI appraise their pain, the ADAPSS (Dean & Kennedy, 2009) is a 33-item questionnaire incorporating six subscales; fearful despondency, overwhelming disbelief, determined resolve, growth and resilience, negative perceptions of disability and personal agency. These six sub scales can be combined into two sub scales: catastrophic negativity and resilience, and these were used in this study. Participants are asked to state how much they agree with each statement using a 5-point Likert scale with the end points 1 = totally disagree and 5 = totally agree. The scores for each subscale range from 19 to 95 for catastrophic thinking and from 14 to 70 for resilience. The ADAPSS, which was designed specifically for the spinal cord injuries population, has been found to have good validity, reliability and internal consistency ($\alpha = 0.70 - 0.86$; Dean & Kennedy, 2009).

4. **Pain Self-Perception Scale (PSPS)**

The PSPS (Tang, Salkovskis, & Hanna, 2007) is a 24-item scale assessing mental defeat in relation to pain. Participants are asked to think about a recent episode of severe pain and state how true each statement was for them during that period of pain using a 5-point Likert scale with the end points 0 = not at all and 4 = very strongly. The total score ranges from 0 - 96, with a score greater than 23 indicative of high mental defeat (Tang et al., 2010). The PSPS has good test-retest reliability and internal validity (Tang, Salkovskis, & Hanna, 2007) in the able-bodied chronic pain population, but has not been used for people with SCI.

5. **Chronic Pain Acceptance Questionnaire (CPAQ)**

The CPAQ (McCracken, Vowles & Eccleston, 2004) is a 20-item questionnaire assessing the degree to which pain influences behaviour (activity engagement) and the degree of effort put into controlling pain (pain willingness). Items include “I am getting on with the business of living no matter what my level of pain is” (activity engagement), and “I need to concentrate on getting rid of pain” (pain willingness). Using a 7-point Likert-scale participants rate how true each statement is for them, with end points 0 = never true and 6 = always true. The total score ranges from 0 to 120. Greater acceptance of pain generally is indicated by a higher total score. The activity engagement subscale has scores ranging from 0 to 66, and the pain willingness subscale has scores ranging from 0 to 54. Higher scores represent higher engagement in activities despite pain and a greater willingness to accept the presence of pain without trying to control it. Support for the reliability and validity of the CPAQ in a chronic pain sample has been published by Vowles, McCracken, McLeod and Ecclestone (2008). Additionally, Wicksell, Olsson and Melin (2009) found it had strong internal consistency ($\alpha = 0.83 - 0.91$). It has also been validated for use in a spinal cord injured sample where a good model fit of the two-factor structure was indicated by the Tucker-Lewis Index = .92 and the Bentler Comparative Fit index = .93. Internal consistency and reliability were found to be strong with Cronbach’s alphas of .90 for the total score, and .86 for each subscale of

activity engagement and pain willingness (Kratz, Ehde, Bombardier, Kalpakjian, & Hanks, 2017).

6. **Hospital Anxiety and Depression Scale (HADS)**

The HADS (Zigmond & Snaith, 1983) is a 14-item scale which is able to detect and assess the severity of clinical levels of anxiety and depression without scores being affected by physical symptoms. Scores for each sub-scale range from 0 to 21 with a cut-off for clinical levels set at 8 or higher (Olssøn, Mykletun & Dahl, 2005). A review by Bjelland, Dahl, Haug and Neckelmann (2002) assessing its reliability and validity found that it has good internal consistency; α = .67 - .90 for the depression scale and α = .68 - .93 for the anxiety scale. Good internal consistency and content validity were also found in an evaluation of the HADS in a community sample of people with a SCI (Woolrich, Kennedy & Tasiemski, 2006).

Table 4. The questionnaires used at each time point.

Measure	Time 1	Time 2	Time3
S-LANSS	✓	✓	✓
MPI-SCI A	X	✓	✓
MPI-SCI B	✓	✓	✓
MPI-SCI C	X	✓	✓
PSS-10	✓	✓	✓
PCS	✓	✓	✓
ADAPSS	✓	✓	✓
PSPS	✓	✓	✓
CPAQ	✓	✓	✓
HADS	✓	✓	✓

9.2.2 **Cortisol Analysis**

One of the most effective ways of analysing cortisol is through saliva. In saliva most of the cortisol is unbound to proteins and biologically active, whereas in

blood the majority is bound to serum proteins (Aardal & Holms, 1995). Additionally, salivary flow rate and the freeze-thaw cycles during analysis have little effect on cortisol (Garde & Hansen, 2005). Serum cortisol levels have consistently and reliably been estimated by salivary cortisol (Dorn et al, 2009), and it is a minimally intrusive way of collecting and analysing it (Kirschbaum & Hellhammer, 1989). Concentrations of cortisol in the saliva samples were analysed using an enzyme-linked immunoassay kit which measures micrograms per decilitre of salivary cortisol.

9.2.2.1 Apparatus

- Microtitre plate coated with monoclonal anti-cortisol antibodies.
- 6 x 500 microlitre (µL) vials of cortisol standards containing buffer, preservative and cortisol in the following micrograms per decilitre (µg/dL) quantities; 3.0, 1.0, 0.333, 0.111, 0.037, and 0.012.
- 2 x 500 µL vials, one each of a high and low cortisol control containing cortisol, buffer and preservative.
- 100 millilitres (mL) washer buffer concentrate containing phosphate buffer, detergent and preservative.
- 60 mL assay diluent containing phosphate buffer, pH indicator and preservative.
- 1 x 50 µL vial cortisol enzyme conjugate concentrate containing cortisol conjugated to HRP and preservative.
- 25 mL tetramethylbenzidine substrate solution.
- 12.5 mL stop solution containing sulphuric acid.
- 2 x non-specific binding (NSB) wells without anti-cortisol antibody to be used as blanks.
- Aliquot tubes.
- Pipette and pipette tips to deliver 15 and 25 µL quantities.
- Multichannel pipette and pipette tips to deliver 50 and 200 µL quantities.
- Pipette and pipette tips to deliver 5 mL quantities.
- 50 mL disposable tube.
- Deionized water.
- Centrifuge to spin saliva from saliva collection swabs and to send mucins to

the bottom of the saliva sample.

- Plate rotator to mix the contents of the microtitre plate.
- Reagent reservoirs.
- Plate reader with 450 nanometer (nm) filter used to read the optical density of the microtitre plate.
- Softmax Pro computer software used to analyse the results of the plate reader.

9.2.2.2 Principles

Participants were asked to avoid exercise, food and drink in the hour prior to taking the saliva sample. This is important as exercise increases cortisol concentration levels and food in general can alter the pH and bacterial levels of the sample (Salimetrics, 2011). Dairy products can cross react with the anti-cortisol antibody in the assay used for analysis (Salimetrics, 2011).

The kit consists of a microtitre plate coated with monoclonal antibodies to cortisol. Standards containing cortisol and the saliva samples are added to the plate. The cortisol in the saliva samples and the cortisol in the standards compete with cortisol linked to horseradish peroxidase (HRP) for the antibody binding sites. After a period of incubation the tray is washed and only bound components remain. The substrate Tetramethylbenzidine (TMB) is added to the plate which reacts with the peroxidase enzyme, producing a blue colour. This turns to yellow once sulphuric acid is added to stop the reaction. The amount of cortisol peroxidase is measured by the intensity of the colour, its optical density. This is inversely proportional to the amount of cortisol present.

9.2.2.3 Cortisol Concentration Analysis: Procedure

The enzyme immunoassay kit was removed from the fridge for one and a half hours before use to enable it to reach room temperature. The saliva samples were thawed at room temperature before being spun in a centrifuge at 1,500 relative centrifugal force (rcf) for fifteen minutes to send the mucins to the bottom of the tubes. 25 µL of the standards, the high and low controls and the

samples were pipetted into the wells of the microtitre plate in duplicate. 25 µL of assay diluent was pipetted into the two NSB wells. 24 ml of assay diluent was placed in a 50 ml tube and 25 µL of conjugate was added to it. This was gently mixed before adding 200 µL to each well (except the NSB wells) using the multichannel pipette. The plate was then covered and mixed on the plate rotator at 500 revolutions per minute (rpm) for five minutes, after which it was left to incubate at room temperature for 55 minutes. After incubation the plate was emptied, and washed four times with a solution of one part washer buffer to nine parts deionized water. After each wash the plate was thoroughly blotted on paper towels until the towel showed no damp mark. 200 µL of TMB was placed in all cells using a multichannel pipette and the plate was covered and mixed on the plate rotator at 500 rpm for another five minutes. It was left to incubate in the dark for 25 minutes at room temperature. 50 µL of stop solution was then added to each cell and the plate covered and mixed at 500 rpm for a final time for three minutes. The plate was then immediately read in the plate reader at 450 nm. This protocol was followed for each analysis undertaken.

9.3 Design

The out-patient study consisted of a cross-sectional study undertaken with spinal cord injured participants in the community. A similar multiple assessment-point design was carried out longitudinally with spinal cord injured in-patients at the NSIC at Stoke Mandeville. The study has ISRCTN registration number ISRCTN26442074.

9.3.1 Procedure

9.3.1.1 Out-Patient Study

The CONSORT diagram below (Figure 18) shows the procedure used to collect data from out-patients. Out-patients of the NSIC meeting the inclusion criteria were sent an information pack containing an information sheet, an invitation to participate, a consent form and a reply paid envelope. Those

people who returned the consent form were telephoned and asked if they had any further questions and whether they would prefer to complete paper versions of the questionnaires or an on-line version using Survey Monkey. Either the online link or the questionnaire pack, along with a kit for taking their saliva samples and reply paid envelopes were sent to participating out-patients. One follow-up letter was sent as a reminder to those who did not return a consent form. Individuals who heard about the study through the SIA and who were interested in participating contacted the lead researcher who sent them the paper version of the questionnaires or the online link, the saliva sample kits and reply paid envelopes.

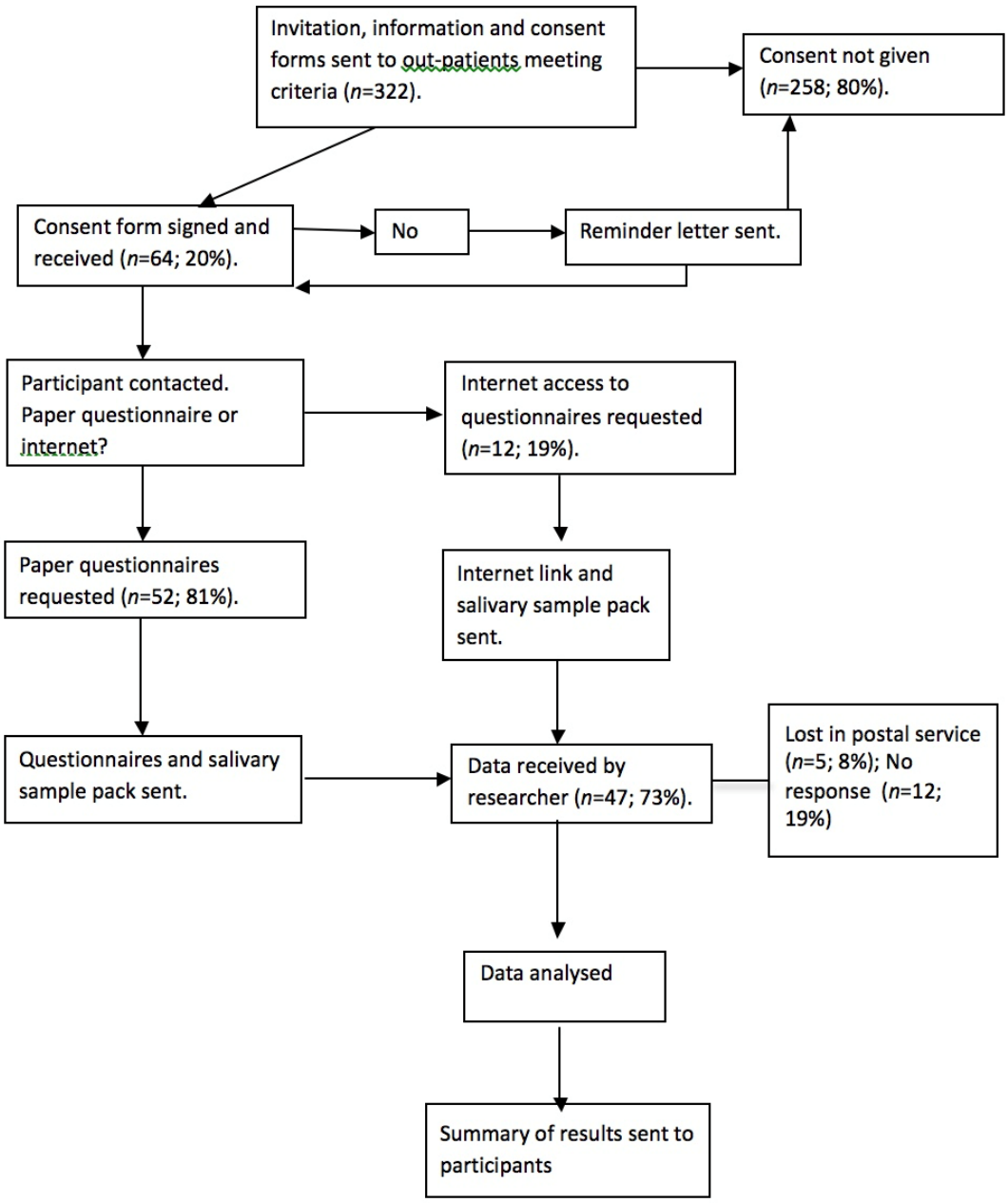

Figure 18. Procedure for collecting data from the out-patient participant group.

Participants were given an instruction sheet giving clear guidance about how to provide the saliva samples. Cortisol production has a circadian rhythm. Levels peak as a response to waking, then sharply decline, with the lowest concentration levels occurring at night (Pruessner et al., 1997). Collecting cortisol during the CAR (CAR) has a number of problems associated with it. The time of the cortisol peak will vary amongst individuals relative to their normal wake up time (Saliva Collection and Handling Advice, Salimetrics,

2009). If individuals are waking regularly throughout the night, which is feasible if they are experiencing pain, then it cannot be assumed that the saliva sample collected reflects the CAR accurately. For CAR samples to be meaningful they need to be taken at very precise time points (Stalder et al., 2016), which is hard to control when participants are taking samples themselves remotely. Stalder et al. (2016) report widespread sampling inaccuracies related to the time the sample was taken, with participants regularly delaying taking the sample by more than 15 minutes, and sometimes up to 40 minutes. This has a large impact on estimates of CAR. Added to this, and as previously stated (see Section 5.3 Biological Theories of Pain), the CAR is not a reliable biomarker of changes caused by stress or as an indication of HPA (HPA) axis activity (Clow, Hucklebridge, Stalder, Evans, & Thorn, 2010). The peer reviewed website Lab Tests On Line (American Association for Clinical Chemistry, 2013) suggests that salivary cortisol should be tested at 11pm when it is at its lowest. This is not always possible as people at home may go to bed earlier than this and it is difficult to access patients in hospital at this time of night. However, cortisol concentration levels are at a similar level and relatively stable between 3pm and 6pm making it a suitable alternative.

In their Saliva Collection and Handling Advice sheet, Salimetrics (2009) recommend that, most importantly, the sample collection should be made at standardised times and the date and time of collection recorded. Therefore, all samples, for in-patients and out-patients, were collected between 3pm and 6pm. Because pain medication can reduce saliva secretion two saliva samples were requested to ensure sufficient saliva was collected for analysis. Participants completed a form confirming that they had not had food or drink or engaged in strenuous activity in the preceding hour nor had they had alcohol in the preceding 12 hours. They were asked to keep their saliva samples in a refrigerator overnight and to post the samples and the questionnaires (if paper ones were completed) to the University of Buckingham the morning after the saliva samples were taken. Appropriate stamped and addressed packaging was provided to enable them to do this easily. Questionnaires were sent to the lead researcher and saliva samples were sent directly to the laboratory. As

soon as they were received, the samples were spun in a centrifuge at 3000 rpm for fifteen minutes, aliquoted and frozen at -80 degrees centigrade. Freezing the samples precipitates the mucins in the saliva.

9.3.1.2 In-Patient Study

Figure 19 shows the procedure used to collect data from in-patients. In-patients at the NSIC were approached and given verbal information about the study. If they were interested in participating they were provided with a written information sheet and given a week to consider whether they would like to take part or not. After one week they were approached again and asked if they would like to be involved in the research. If they confirmed that they would, an appointment was made at a time convenient to the patient and one that fitted in around their other activities.

In-patient participants were asked to complete the questionnaires and to provide two salivary cortisol samples on three occasions. The first assessments and saliva samples were taken whilst the participants were in-patients at the NSIC and the following two assessments and samples were taken six and nine months later. Identical packs as those sent to out-patients were sent to participants who had returned home by that time, with the option of completing paper or online questionnaires using Survey Monkey. Whilst patients were in hospital, the researcher administered all questionnaires and took the saliva samples using a cotton swab placed under the tongue for two minutes. As with the out-patients sample, saliva samples were always taken between 3pm and 6pm, kept in a refrigerator over night and then spun in a centrifuge at 3000 rpm for fifteen minutes, aliquoted and frozen.

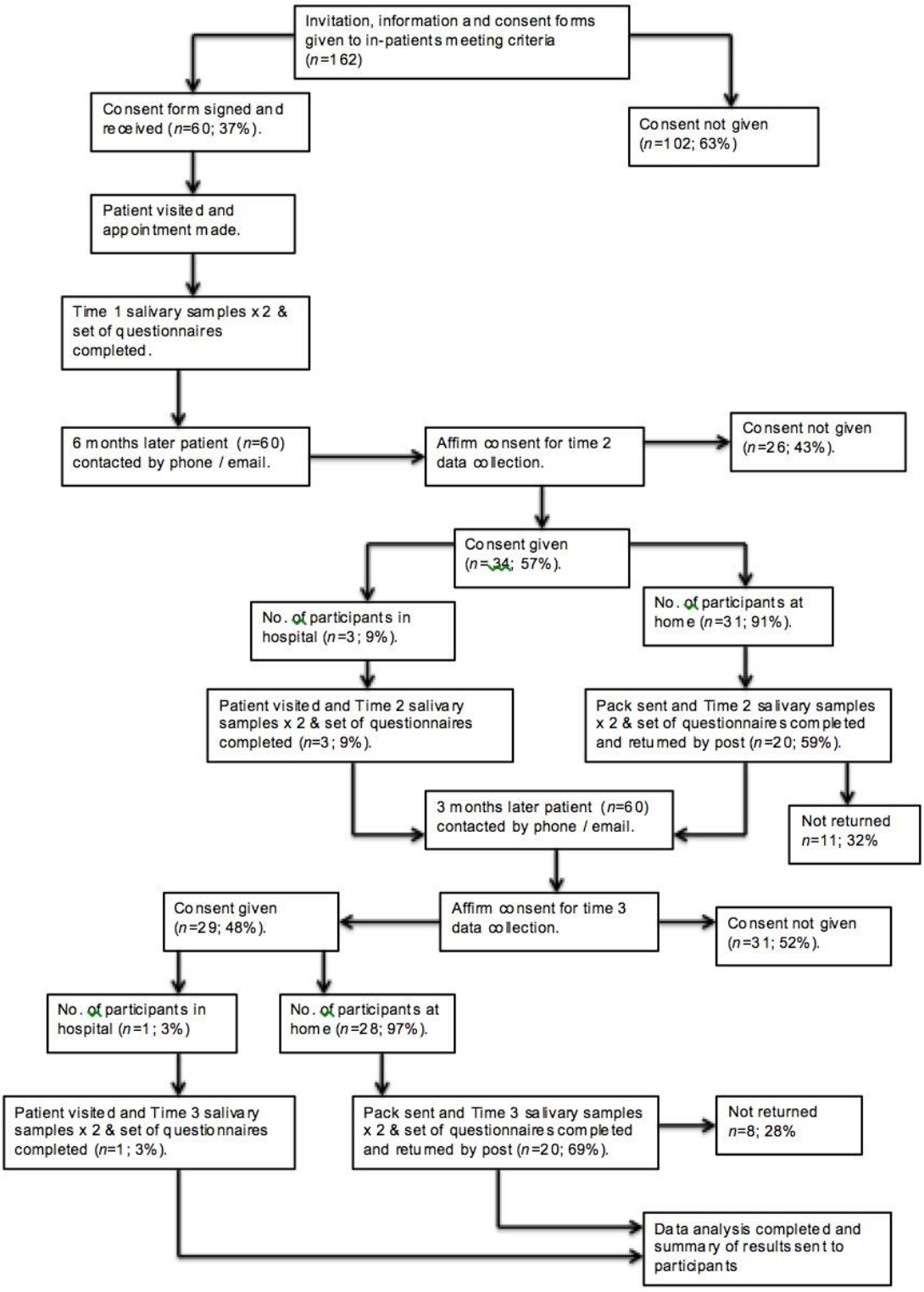

Figure 19. Procedure for collecting data from the in-patient participant group.

9.4 Ethics

All patients were provided with a detailed information sheet, which fully explained the purpose of the research, and what would be involved in participating in it. No debriefing was therefore necessary. Patients gave informed consent to participate in the study, signing a consent form to confirm this. For participants with tetraplegia who were unable to sign the consent form themselves, a member of their family or a member of the NSIC staff signed on their behalf. It was made clear to all those agreeing to participate that they could withdraw from the study at any time without it affecting their treatment in any way. This was in the written information and was confirmed verbally with each participant.

This study was designed with a view to maximising useful information obtained whilst minimising the burden to the participants through the time taken to complete questionnaires. This was possible by the choice of measures which provided maximum information, whilst being straightforward and quick to complete. The questionnaires were piloted by two healthy volunteers and two people with a SCI from the SIA and feedback confirmed the above. Professor Paul Kennedy, Consultant Clinical Psychologist at the NSIC, approved the questionnaires as being suitable for the population involved. Whilst it was not anticipated that the questionnaires would cause significant distress, where low levels of distress were experienced, participants were offered the option of not completing them or of taking a break for as long they needed. Participants were also made aware of the option of seeing a member of the clinical psychology team at the NSIC. Additionally, it was agreed with the clinical psychology team that if the researcher had any concerns about the psychological wellbeing of any participant a member of the team would be informed, and this information was also given to participants in advance of them signing the consent sheet. There were no occasions when this action was necessary. Other than in this instance, confidentiality was assured.

To gather the saliva samples, a cotton swab is placed under the tongue. It was considered that this would provide a choking hazard to people with limited or

no use of their hands. For this reason children's swabs were used which are longer and are placed under the tongue like a thermometer, with the end remaining outside of the mouth. In this way the experimenter was able to remove the swab and ensure choking did not occur, therefore, there was no risk of physical harm to patients.

An in-patient and out-patient log was kept to track when questionnaires etc. had been sent to and returned from participants. This was kept locked in a filing cabinet in a secured office at the University of Buckingham, as was data received from each individual. Participants were given an identification number so that when their data was transferred to an Excel spreadsheet and onto SPSS files, no identifying information was attached to it. Only the researcher and her supervisor had access to personal information about the participants and only they could associate questionnaire responses and cortisol concentration levels to specific individuals. Saliva samples were labelled with participant identification numbers only and as such were not identifiable to any individual.

Ethical approval for the study was granted by the NHS Health Research Authority NRES Committee South Central - Oxford C (Ref: 13/SC/0457), with on-site approval given by the Buckinghamshire Healthcare NHS Trust's Research and Development Office (Ref: RXQ 584) and the NSIC Research Board. Ethical approval was also granted by The University of Buckingham School of Science and Medicine Ethical Committee.

9.5 Statistical Analysis

Before the testing of the hypotheses commenced, a number of analyses were carried out. These examined whether demographic variables contributed to drop out rates in the in-patient longitudinal study, the reliability of questionnaires, and compared demographic variables to each questionnaire. To analyse whether demographic variables were associated with drop-out rates *t*-tests were used for the comparison of two variables, and ANOVAs were used when there were more than two variables to compare. Where data was

categorical Chi Square tests were carried out providing the number of frequencies met the requirements of the test. To test the reliability of the questionnaires in each patient group, Chronbach's Alpha was used. In order to compare demographic data to each questionnaire for the in-patient time 1 and out-patient groups *t*-tests, ANOVAs and correlations were used. To assess the effect sizes in the *t*-tests and ANOVAs, Cohen's D and Omega squared were used respectively. Gabriel and Games-Howell post hoc tests were used when equal variance between groups could not be assumed.

In the past two decades statisticians have been critical of the methods used to deal with missing data (Schafer & Graham, 2002; Schlomer, Bauman & Card, 2010; Dong & Peng, 2013), and psychological and social research have been areas particularly targeted for such criticism (Dong & Peng, 2013; Sclomer et al., 2010). It is suggested that failing to properly impute missing data results in inaccurate and potentially skewed or biased results (Dong & Peng, 2013; Schafer & Graham, 2002). However, the two most widely used methods, pairwise deletion and listwise deletion, are said to be particularly inefficient and biased (Rubin, 1987). So poor are they considered to be that the American Psychological Association Task Force on Statistical Inference have stated explicitly that they should not be used (Wilkinson and the Task Force on Statistical Inference, 1999, p. 598). Therefore, following these guidelines, patterns of missing data were first analysed using Littles Missing Completely At Random (MCAR) test. There are three patterns of missingness. Missing completely at random describes missing data that have no pattern, and that have no relationship to other study variables. Missing at random refers to missing data that are related to other observed data but not to other missing data. For example, an individual may not have responded to a question about pain, not because they are in a great deal of pain, but because they are experiencing high mental defeat. Not missing at random describes missing data that has a pattern and is likely to be related to whether the person would have scored high or low on that variable had they responded. In this instance the individual does not respond to a question about pain, because of the pain they are experiencing. When data are missing completely at random various imputation methods can be used. The most highly recommended methods are

Multiple Imputation, Expectation Maximisation and Full Information Maximum Likelihood (FIML; Schafer & Graham, 2002; Schlomer, Bauman & Card, 2010; Dong & Peng, 2013). As FIML is not available using SPSS, Multiple Imputation and Expectation Maximisation were used in the analysis of missing data that were missing completely at random.

Multiple imputation has three steps. Firstly, it imputes the missing values multiple times using the observed data to generate plausible values and uses this data to create five additional data sets. Next, standard statistical procedures are used to analyse each data set separately. This produces slightly different parameter estimates. In the final step, these estimates are pooled to produce a single value for the parameter and its standard error. Multiple imputation is one of the preferred methods of dealing with missing data because the standard error incorporates the between imputation uncertainty (uncertainty caused by the treatment of missing data) into the within imputation uncertainty (inherent uncertainty found in any method of estimation). This provides a larger, more accurate standard error, minimising bias found in single imputation methods (Dong and Peng, 2013).

Expectation maximisation is a maximum likelihood approach, which uses observed data to estimate parameters, and this in turn is used to estimate the missing data. EM is an iterative process. Once the parameters have been estimated from the observed data, regression methods are used to determine the values of the missing scores (expectation). Next, new values for the parameters are estimated using both the original data and the newly imputed data (maximisation). These steps are repeated until there is little change in the estimated values between each iteration. Both of these ways of dealing with missing data have been widely recommended (e.g. Schafer & Graham, 2002; Schlomer, Bauman & Card, 2010; Dong & Peng, 2013).

A variety of statistical analyses were used to test hypotheses one to six. To analyse the difference between in-patient T1 and out-patient samples and between in-patient Time 3 (T3) and out-patients (Hypotheses 1a and 1b) on each variable *t*-tests were used. Cohen's D was used to calculate the effect

sizes.

Multiple regressions using the ‘forced entry’ method were carried out to analyse whether psychological (hypotheses 2a, b and c and 3a, b and c), social (hypotheses 4a, b and c) and biological (hypotheses 5ai, aii and aiii) variables would predict pain-specific outcome measures. In-patients T1 only completed the pain intensity rating and not the life interference or distress scales because the nature of the questions was not relevant whilst people were still in hospital. Because of this, analysis of in-patients T1 for hypotheses 2 - 5 was only included where pain intensity was the outcome measure. Where *t*-tests had found no difference between in-patient T1 and out-patient scores (see Hypothesis 1a and 1b results) these were collapsed and used as a combined sample for hypotheses 2 - 5 when pain intensity was the outcome measure. The analysis for hypotheses 1 - 5 was carried out on a data set that had multiple imputation applied to deal with the missing data. SPSS does not give the pooled result on all outputs for multiple regression analysis when multiple imputation is used. When this is the case, the range of results across the original data set and each imputation model is given.

Correlation analysis was carried out to assess the relationship between each of the variables and cortisol concentration levels (hypotheses 5bi, bii, biii and biv). Kendall’s tau was used as the cortisol data set had outliers and tied ranks, and was not normally distributed. Kendall’s tau has the added benefit of providing a better estimate of the population when sample sizes are smaller (Field, 2018). To carry out the longitudinal analysis on the in-patient group over the three time points (hypothesis 6a) one-way repeated measures ANOVAs were used. Partial eta squared was used to assess effect sizes. To analyse the relationship between time since injury and each of the variables (hypothesis 6b) Spearman’s Rho correlations were used as the time since injury data were not normally distributed. The analyses for hypotheses 5b, 6a and 6b were carried out on data sets where expectation maximisation had been applied to deal with missing data. This was because data that was not normally distributed were used in hypotheses 5b and 6b, therefore bootstrapping needed to be applied and this is not possible on multiply

imputed data sets. Additionally, repeated measures ANOVAs were used for hypothesis 6a and multiple imputation is not compatible with this form of analysis in SPSS.

Power analyses using G*Power 3.1 were carried out to determine appropriate sample sizes for multiple regression analyses. An alpha = .05 and power = .80 was used in the calculations. Effect sizes in the literature vary quite considerably so both medium and large effect sizes were used to calculate sample sizes for the multiple regressions. The analyses identified that where one predictor was used a sample of between 25 - 55 was required, where three predictors were used a sample of between 36 - 77 was required, where four predictors were used a sample of between 40 - 85 was required and where five predictors were used a sample of between 43 - 92 was required. For the analysis using ANOVAs, to obtain a power of .80, a sample size of 158 is necessary. Lastly, the power analysis identified that for the t-tests, a total sample size of 106 was necessary, with groups of 41 and 65 participants.

10 Chapter 8 - Results

10.1 Stage 1 Analysis

10.1.1 Analysis of Drop Out Rates

ANOVAs were carried out to examine whether there were any differences between the in-patient groups at time 1, time 2, and time 3, on time since injury, pain intensity or age, and a *t*-test was carried out to see if there were gender differences. None of these were significant, suggesting that these demographic variables did not contribute to dropout rates in the in-patient longitudinal study. Further analysis of demographic variables and dropout rates was not possible. The data was categorical and therefore Chi Square tests needed to be used, however, the minimum requirement is for frequencies to be greater than five in 80% of cases and this assumption was not met. Observed frequencies, expected frequencies and percentages are shown in Appendix 2.

10.1.2 Questionnaire Reliability

Reliability of each of the questionnaires used, for each participant group (out-patients and in-patients Times 1, 2, and 3), was measured using Cronbach's Alpha. The Cronbach's α for each can be seen in Table 4. The ADAPSS, CPAQ, HADS, PSPS, PSS, and the MPI C scale all had high reliabilities, with Cronbach's α ranging from .738 - .984. The PCS mostly had high reliability on the total score and each sub-scale (Cronbach's α = .812 - .951) but on the magnify sub-scale for in-patients Times 2 and 3 Cronbach's α was lower at .673 and .556 respectively. Reliability of the MPI A was high across all groups (α = .723 - .912) apart from Life Control and Pain Severity for the in-patient Time 2 group which had Cronbach's α of .550 and .658 respectively. The MPI B had high reliability for the out-patient group across each sub-scale (α = .752 - .919). The reliability varied across the in-patient groups with Cronbach's α ranging from .552 - .908. The LANSS had lower reliability across all groups (Cronbach's α = .517 - .676). High reliability has been demonstrated in each of

these questionnaires in previous studies (see section 6.3.2) and whilst Kline (1999) states that values of .7 and .8 are generally considered to be acceptable values, he goes on to state that lower values can be expected when measuring psychological constructs because of the diversity contained within them. This supports the view of Nunnally (1978) who suggests that values as low as .5 are sufficient to suggest reliability.

10.1.3 Assumptions of the Linear Model

Normality of data across the different questionnaires and patient groups was varied as was expected in a sample of spinal cord injured patients. Additionally, the cortisol data set had outliers. Field (2018) suggests that removing outliers should only be done if it is clear that the outlier does not come from the population being examined. Therefore, outliers and normality were dealt with by using bootstrapping, as recommended by Field (2018), where the method of dealing with missing data made this possible. Bootstrapping is not compatible with Multiple Imputation (MI) when using SPSS but is with Expectation Maximisation (EM). Additionally, Kendall's Tau was used for the correlation analysis involving cortisol measures as this type of correlation analysis deals better with outliers and tied ranks. Where the multiple regression analyses were concerned, assumptions of additivity and linearity, independent errors, collinearity, and homocedasticity were met.

Table 5. Cronbach's Alpha Values for Questionnaires and Their Sub-Scales

Measure	Out-patient α	In-patient 1 α	In-patient 2 α	In-patient 3 α
ADAPSS				
Negativity	.908	.894	.928	.852
Resilience	.843	.886	.940	.928
CPAQ Total	.915			
Engagement	.904	.877	.866	.907
Pain	.900	.860	.884	.905
Willingness		.820	.869	.826
HADS				
Depression	.860	.691	.738	.765
Anxiety	.823	.840	.820	.775
PSPS Total	.984	.974	.977	.979
PSS Total	.841	.887	.937	.883
PCS Total	.951	.916	.921	.933
Ruminate	.924	.850	.890	.870
Magnify	.827	.812	.673	.556
Helplessness	.922	.855	.841	.913
MPI A				
Life Interference	.912		.821	.845
Support	.749		.869	.865
Life Control	.745		.550	.797
Pain Severity	.841		.658	.783
Distress	.857		.811	.723
MPI B				
Responses	.752	.587	.858	.659
Distracting	.919	.849	.908	.858
Negative	.759	.552	.760	.650
Solicitous				
MPI C				
Activities	.857		.881	.892
Reduced by	.889		.946	.972
Pain				
LANSS	.676	.616	.517	.523

Note: Figures are based on small sample sizes.
ADAPSS = Appraisals of disability: Primary and secondary scale; CPAQ = Chronic pain acceptance questionnaire; HADS = Hospital anxiety and depression scale; PSPS = Pain self-perception scale; PSS = Perceived stress scale; PCS = Pain catastrophizing scale; MPI = Multidimensional Pain Inventory; LANSS = Leeds assessment of neuropathic symptoms and signs.

10.1.4 Missing Data Adjustments

The pattern of missing data was analysed using Littles Missing Completely At Random (MCAR) test. This was not significant, $X^2(2446) = 693.678$, $p = 1.000$, suggesting that the missing data was missing completely at random. The amount of missing data is displayed in Figure 20, which shows that overall, 1.76% of data was missing from the in-patient time one and out-patient data sets, and Figure 21, showing that 27.89% of data was missing in total from the in-patient longitudinal data set.

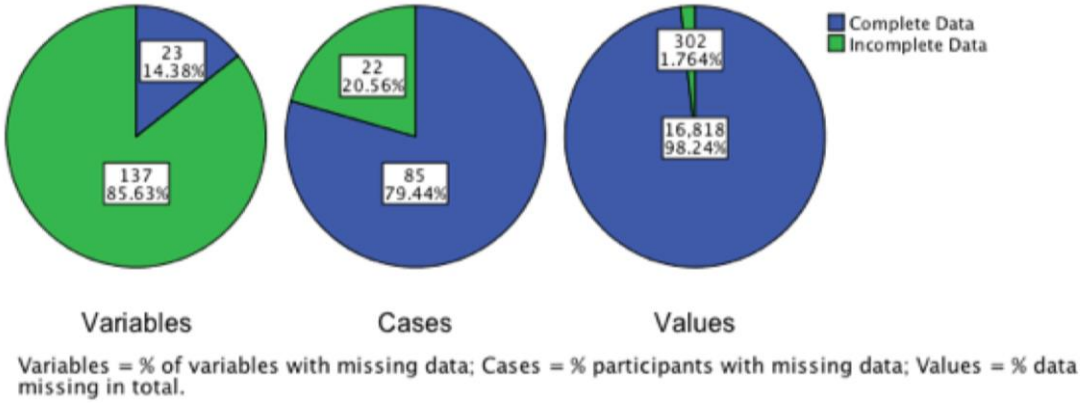

Figure 20. Overall summary of missing values from in-patient time 1 and out-patient data sets.

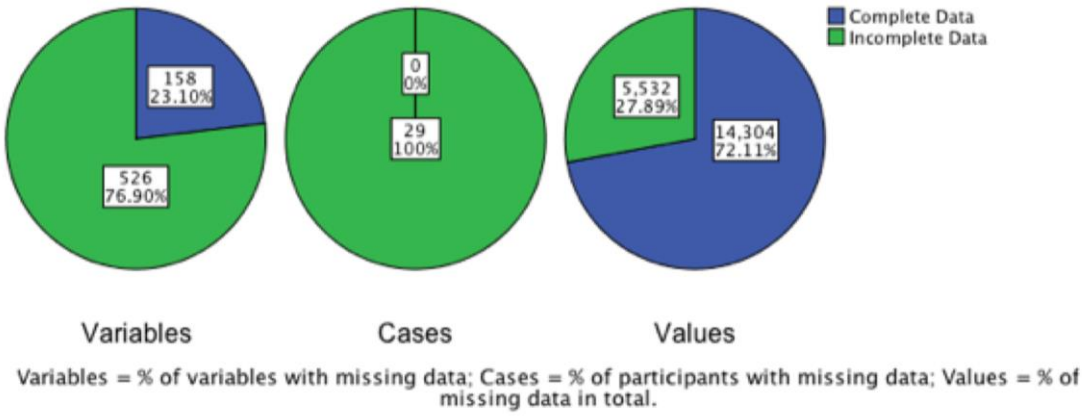

Figure 21. Overall summary of missing values from in-patient longitudinal data

set.

Given the total amount of missing data, and that the missing data was found to be missing completely at random, multiple imputation was used to impute missing data where this was compatible with the type of analysis being used. Where the type of analysis was not compatible with multiple imputation, then expectation maximisation (EM) was used instead.

10.1.5 Analysis of Demographic Data

Demographic data (age, sex, education level, relationship status, time since injury, injury level, injury cause, injury type and neuropathic or nociceptive pain) for in-patient Time 1 (T1) and out-patient groups was compared to each questionnaire, either using *t*-tests, correlations or one-way ANOVAs. Most results for the in-patient T1 group were not significant, indicating that demographic variables were not associated with differences in the outcome variables. However two results were significant: A one-way ANOVA found a significant effect of relationship status on pain catastrophizing, $F(5, 54) = 2.69$, $p = .030$, $\omega^2 = 0.12$. This represents a medium to large effect using omega squared. Post hoc tests could not be carried out because one group had just one participant. A Pearson correlation showed a significant negative relationship between age and pain catastrophizing, $r = -.260$, 95% BCa CI [-.480, -.018], $p = .045$, suggesting that older people were less likely to engage in catastrophic thinking.

Most results for the out-patient group were also not significant, but there were some exceptions. Age was negatively correlated with activity levels (MPI C) and this relationship was significant, $r = -.321$, 95% BCa CI [-.537, -.062], $p = .028$, suggesting that as age increased amount of activity decreased. On average, women were more likely to experience pain-related distress ($M = 10.41$, $SE = .86$) than men ($M = 7.23$, $SE = .85$) and this difference, -3.178, BCa 95% CI [-5.160, -.905], was significant $t(45) = -2.390$, $p = .021$. This represented a large effect of $d = -0.755$, CI [-1.384, -0.127]. A one-way

ANOVA compared education level achieved with degree of mental defeat. The result was significant, $F(5, 40) = 2.47$, $p = 0.48$, $\omega^2 = 0.14$, which represents a large effect size. The Games-Howell post hoc test was used for pairwise comparisons as equal variance between groups cannot be assumed. This showed that only the means for GCSE ($M = 48.84$) and A'Level ($M = 18.56$) were significantly different ($p = .021$), suggesting that people educated to GCSE level were more likely to experience mental defeat than people who continued with their education to A'level.

One-way ANOVAs also demonstrated an effect of relationship status on the degree to which pain reduced activity levels, $F(4, 42) = 3.061$, $p = .027$, $\omega^2 = 0.14$, and on the degree to which pain interfered with life, $F(4, 42) = 2.76$, $p = .04$, $\omega^2 = 0.13$. Both effect sizes are large. However, Gabriel and Games-Howell post hoc tests are not consistent. For the effect of relationship status on pain reduced activity levels Games-Howell reported no significant paired comparisons, whereas Gabriel reported significant differences between widowed ($M = 110$) and single ($M = 26.82$) participants, $p = .006$, between widowed and married ($M = 38.4$) participants, $p = .009$, and between widowed and divorced ($M = 36.25$) participants, $p = .029$, where in each case being widowed was more closely associated with a reduction in activities because of pain.

For the effect of relationship status on life interference from pain Gabriel reported no significant paired comparisons whereas Games-Howell reported a significant difference between married ($M = 28.54$) and single ($M = 16.27$) participants, $p = .035$, suggesting that greater life interference from pain is more closely associated with being married than being single. Gabriel is a recommended post hoc test when sample sizes are different but if the difference is too great, it can be too liberal (Field, 2018). Games-Howell is recommended when sample sizes and population variances are unequal, but if sample sizes are small it can also be too liberal (Field, 2018). In this instance, Games-Howell is likely to be the more conservative given the large difference in group sizes.

No further significant results were found. As the majority of these analyses were not significant, and where there was a significant result post hoc tests were not consistent, the demographic variables were not carried forward to the regression analysis.

A chi square analysis was carried out to see whether the out-patient and in-patient samples differed in their injury type (tetraplegia and paraplegia). There was no difference between the in-patient and out-patient groups on injury type, $\chi 2$ (1) = .0006, p = .937, 95% CF [.43, 2.12]. The effect odds ratio of 0.97 is close to one suggesting that in-patient and out-patient groups have a similar number of people with tetraplegia and paraplegia. Given this similarity between samples, it is one aspect that can be ruled out of explaining any differences found between the groups in the inferential analysis.

10.2 Inferential Analyses of Results

10.3 Hypothesis 1a and 1b – Results

10.3.1.1 In-Patients Time 1 and Out-Patients (Hypothesis 1a)

To analyse the difference between in-patient T1 and out-patient samples on each of the variables measured, *t*-tests were used. Effect sizes were calculated using Cohen's D. Multiple Imputation was used to impute missing data. Table 5 lists where differences were and were not found between the two groups for each variable.

On average, out-patients displayed higher catastrophic negativity with regard to their SCI (on the ADAPSS) (M = 65.97, SE = 2.05) than in-patients (M = 60.10, SE = 2.02). This difference, -6.55, 95% CI [-11.592, -.151], was significant, t(381748) = -2.01, p = .04 with a small to medium effect size of d = -0.42. In contrast, out-patients on average had lower determined resilience with regard to their SCI (M = 51.48, SE = 9.38) than in-patients (M = 55.63, SE = 11.21).). This difference, 3.99, 95% CI [.039, 7.955] was also significant, t(302394) = 1.98, p = .05, and this also had a small to medium effect of d =

0.40.

The CPAQ measures the degree to which people engage with life activities and their willingness to accept pain as part of their life. On average in-patients engaged with life activities to a greater degree (*M* = 41.83, *SE* = 1.68) than out-patients (*M* = 36.54, *SE* = 1.97). This difference, 5.29, 95% CI [0.25, 10.34] was significant, *t*(256003) = 2.06, *p* = 0.04, with a small to medium effect size of *d* = 0.39. In-patients also had a greater willingness to accept life with pain on average (*M* = 27.95, *SE* = 1.48) than out-patients (*M* = 24.93, *SE* = 1.83), however, this difference, 3.02, 95% CI [-1.55, 7.59], was not significant, *t*(123654) = 1.29, *p* = 0.19. This represented a small effect of *d* = 0.25. Across both subscales, on average, in-patients showed greater pain acceptance (*M* = 69.78, *SE* = 2.69) than out-patients (*M* = 61.47, *SE* = 3.27), and this difference, 8.31, 95% CI [0.09, 16.54] was significant, *t*(250969) = 1.98, *p* = 0.04. This, however, only represents a small effect of *d* = 0.38.

Table 6. Where differences between in-patients T1 and out-patients were found or not found on each variable.

Significant differences found	No significant differences found
CPAQ Total score: OP ↓; IP ↑ CPAQ Engagement with life activities: OP ↓; IP ↑	CPAQ Pain willingness
MPIB Solicitous response: OP ↓; IP ↑	MPIB Negative response MPIB Distracting response
ADAPSS Catastrophic negativity: OP ↑; IP ↓ ADAPSS Resilience: OP ↓; IP ↑	HADS Depression HADS Anxiety
	Pain Catastrophizing Scale and sub-scales
	Perceived Stress Scale
	Pain Self-Perception Scale (mental defeat)
	LANSS Pain severity

Note: OP = out-patients; IP = in-patients; CPAQ = Chronic Pain Acceptance Questionnaire; MPIB = Multidimensional Pain Inventory section B; ADAPSS = Appraisals of Disability: Primary and Secondary Scale; HADS = Hospital Anxiety and Depression Scale; LANSS = Leeds Assessment of Neuropathic Symptoms and Signs.

The MPI subscale B measures how a significant other person responds when an individual expresses pain. It catagorizes responses as being distracting, negative or solicitous. There was no significant difference between in-patients and out-patients on distracting and negative responses. However, it was interesting that in-patients significant others' gave more solicitous responses (M = 16.86, SE = 0.79) than out-patients significant others (M = 13.45, SE = 1.09). This difference, 3.41, 95% CI [0.81, 6.01], was significant, $t(801137) = 2.57$, $p = 0.01$ and represents a medium effect of $d = 0.49$. There were no further significant differences between samples on any of the other variables.

10.3.1.2 In-Patients T3 and Out-Patients (Hypothesis 1b)

The difference on each variable between in-patients T3 and out-patients was also measured using *t*-tests. Expectation Maximisation was used to impute missin data. However, because the sample was small, the analysis was underpowered so the results need to be treated with caution. The only significant difference was on the HADS depression scale, where in-patients T3 (*M* = 12.72, *SE* = 0.88) on average had higher depression scores than out-patients (*M* = 9.53, *SE* = 0.70). This difference, 3.19, BCa 95% CI [0.93, 5.42], was significant, *t*(74) = 2.82, *p* = .006, and represents a medium to large effect of *d* = 0.67. No further significant differences were found.

10.4 **Multiple Regression Analysis**

Multiple regression analyses were carried out to see whether the psychological, biological and social variables would predict pain intensity ratings, life interference from pain and pain-related distress. Multiple Imputation was used to impute missing data in all of the regression analyses. A summary of the results can be found in Table 6 below, followed by the detailed results of the analyses of hypotheses two, three, four, and five.

Table 7. Summary of the stage 1 multiple regression analyses results

Predictor	Pain Intensity	Life Interference	Pain-Related Distress
Perceived Stress	-	0	+
Catastrophizing	+	0	0
Mental Defeat	0	0	0
Depression	0	+	+
Anxiety	0	0	0
PCS Rumination	0	0	0
PCS Magnify	0	+	0
PCS Helplessness	+	0	0
Catastrophic Negativity	0	+	+
Resilience	0	-	-
Activity Engagement	0	0	+
Pain Willingness	0	0	0
Distracting Response	0	+	0
Negative Response	0	+	+
Solicitous Response	0	0	0
Cortisol	0	0	0

Note: PCS = Pain Catastrophizing Scale; - = negative relationship; + = positive relationship; 0 = no relationship

10.4.1 Hypothesis 2 - Results

Negative psychological characteristics will predict pain intensity scores, the extent of life interference and levels of distress.

'Forced entry' multiple regressions were carried out to analyse whether negative psychological variables (depression, mental defeat, anxiety, perceived stress, pain catastrophizing and catastrophic negativity) would predict pain-specific outcome measures (pain intensity, life interference and pain-related distress). For the catastrophic negativity sub-scale of the ADAPSS, in-patient T1 and out-patient samples were analysed separately, as *t*-tests showed a significant difference between the scores of the two groups. There were no differences between in-patient T1 and out-patient scores on the other negative psychological variables so the two data sets were combined when the outcome measure was pain intensity.

10.4.1.1 Hypothesis 2ai - Results

Negative predictors of pain intensity (in-patient and out-patient data sets).

In a forced entry regression predicting change in LANSS pain intensity scores, scores of depression, mental defeat, anxiety, perceived stress and pain catastrophizing were force entered in one step. The model was significant, $F(5, 106) = 3.59 - 4.11$, $p = .002 - .005$, (Table 7) and explained between 16.1% and 16.9% of the variance. Two independent variables contributed significantly to the prediction of pain intensity ratings. These were pain catastrophizing that predicted higher pain intensity ratings and perceived stress, which predicted lower pain intensity ratings.

Table 8. Linear model of all negative predictors of pain intensity. 95% confidence intervals reported in parentheses.

	b	*SE B*	Beta	*p*
Constant	5.91 (4.86, 6.93)	0.52		.001
PSS	-0.087 (-0.16, -0.02)	0.036	-.448 - -.320	.014
PCS	0.079 (0.03, 0.12)	0.023	.436 - .501	.001
PSPS	-0.009 (-0.03, 0.01)	0.012	-.132 - -.104	.461
HADS Depression	0.094 (-0.06, 0.25)	0.081	.157 - .314	.243
HADS Anxiety	-0.017 (-0.15, 0.11)	0.066	-.006 -.016	.792

$R^2 = .16$

Note. PSS = Perceived Stress Scale; PCS = Pain Catastrophizing Scale; PSPS = Pain Self-Perception Scale; HADS = Hospital Anxiety and Depression Scale.

10.4.1.2 Hypothesis 2bi - Results

Negative predictors of life interference (out-patient data set).

Scores of depression, mental defeat, anxiety, perceived stress and pain catastrophizing were force entered into a one-step regression model to see if they would predict changes in scores on the MPI A life interference scale. The model was significant, $F(5, 41) = 8.97 - 11.61$, $p = .001$, (Table 8), predicting greater life interference and explaining between 52.2% and 60.4% of variance. Only depression contributed significantly to the prediction of life interference, suggesting that the more depressed an individual is, the greater the life interference from pain will be.

Table 9. Linear model of all negative predictors of life interference. 95% confidence intervals reported in parentheses.

	b	*SE B*	Beta	*p*
Constant	10.78 (2.14, 19.16)	4.271		.012
PSS	-0.338 (-0.87, 0.20)	0.274	-.227 - -.177	.217
PCS	0.256 (-0.07, 0.59)	0.169	.147 - .347	.129
PSPS	0.025 (-0.17, 0.22)	0.098	-.013 - .209	.799
HADS Depression	1.096 (0.06, 2.13)	0.526	.344 - .496	.039
HADS Anxiety	0.556 (-0.61, 1.72)	0.587	.125 - .328	.346

$R^2 = .52 - .60$

Note. PSS = Perceived Stress Scale; PCS = Pain Catastrophizing Scale; PSPS = Pain Self-Perception Scale; HADS = Hospital Anxiety and Depression Scale.

10.4.1.3 Hypothesis 2ci - Results

Negative predictors of distress (out-patient data set).

The same negative factors as in hypotheses 2a and 2b were force entered into a one-step regression model to see if they predicted change in MPI A distress scores. The model was significant, $F(5, 38) = 19.44 - 22.51$, $p = .001$, (Table 9) and explained between 70.3% and 74.3% of variance. Two variables contributed significantly and positively to the prediction of increased pain related distress; depression and perceived stress.

Table 10. Linear model of all negative predictors of pain related distress. 95% confidence intervals reported in parentheses.

	b	*SE B*	Beta	*p*
Constant	-2.061 (-4.40, 0.27)	1.191		.084
PSS	0.288 (0.14, 0.44)	0.077	-.298 - .454	.001
PCS	0.003 (-0.09, 0.10)	0.050	-.056 - .088	.952
PSPS	-0.044 (-0.10, 0.01)	0.028	-.312 - .226	.116
HADS Depression	0.384 (0.10, 0.67)	0.143	.365 - .452	.007
HADS Anxiety	0.308 (-0.01, 0.62)	0.161	.258 - .403	.057

$R^2 = .70 - .74$

Note. PSS = Perceived Stress Scale; PCS = Pain Catastrophizing Scale; PSPS = Pain Self-Perception Scale; HADS = Hospital Anxiety and Depression Scale.

10.4.1.4 Hypotheses 2aii - Results

Perceived stress and pain catastrophizing sub scales as predictors of pain intensity (in-patient and out-patient combined data sets).

Scores from the PSS and the subscales from the PCS were force entered into a one-step regression model to see if they predicted changes in LANSS pain intensity ratings. The model was significant, $F(4,102) = 6.92 - 7.32)$, $p = 001$, (Table 10) and explained between 21.9% and 22.3% of variance. Perceived stress and helplessness were the only variables to contribute significantly to the prediction of pain intensity ratings, with lower perceived stress and increases in helplessness predicting increases in pain intensity.

Table 11. Linear model of perceived stress and catastrophizing as predictors of pain intensity ratings. 95% confidence intervals reported in parentheses.

	b	*SE B*	Beta	*p*
Constant	6.144 (5.12, 7.17)	0.522		.001
PSS	-0.068 (-0.13, -0.01)	0.030	-.273 - -.254	.021
PCS Ruminate	0.018 (-0.11, 0.14)	0.064	.053 - .037	.783
PCS Magnify	-0.139 (-0.30, 0.02)	0.082	-.218 - -.198	.089
PCS Helplessness	0.202 (0.10, 0.30)	0.053	.637 - .614	.001

$R^2 = .22$

Note. PSS = Perceived Stress Scale; PCS = Pain Catastrophizing Scale

10.4.1.5 Hypotheses 2bii - Results

Perceived stress and pain catastrophizing sub scales as predictors of life interference (out-patient data set).

Out-patient responses on the PSS and the PCS were force entered into a one-step regression model to see if they predicted changes in life interference. The model was significant $F(4, 40) = 7.28 - 8.59$, $p = 001$, (Table 11) and explained between 42.1% and 45% of variance. PCS magnify was the only variable to contribute significantly to the prediction of life interference, so that as participants magnified the experience of pain and its impact, they experienced greater life interference from it.

Table 12. Linear model of perceived stress and catastrophizing as predictors of life interference. 95% confidence intervals reported in parentheses.

	b	*SE B*	Beta	*p*
Constant	12.990 (4.23, 21.75)	4.472		.004
PSS	0.065 (-0.45, 0.58)	0.265	.031 - .056	.807
PCS Ruminate	-0.145 (-0.75, 0.47)	0.611	-.060 - -.040	.813
PCS Magnify	1.702 (0.57, 2.83)	0.595	.443 - .451	.004
PCS Helplessness	0.538 (-0.40, 1.47)	0.478	.258 - .307	.260

$R^2 = .42 - .45$

Note. PSS = Perceived Stress Scale; PCS = Pain Catastrophizing Scale

10.4.1.6 Hypotheses 2cii - Results

Perceived stress and pain catastrophizing sub scales as predictors of pain-related distress (out-patient data set).

In a forced entry regression predicting change in pain related distress, scores of pain catastrophizing and perceived stress were force entered in one step. The model was significant, $F(4,42) = 14.99 - 15.90$, $p = .001$, (Table 12) and explained 60% of variance. Perceived stress was the only variable that contributed significantly to the prediction of pain related distress scores, suggesting that perceived stress alone can account for over half of the variance of this pain outcome. It implies that as perceived stress increases, so do levels of distress.

Table 13. Linear model of perceived stress and catastrophizing as predictors of pain related distress. 95% confidence intervals reported in parentheses.

	b	*SE B*	Beta	*p*
Constant	-0.924 (-3.59, 1.74)	1.362		.497
PSS	0.427 (0.27, 0.58)	0.081	.031 - .056	.001
PCS Ruminate	-0.080 (0.45, 0.28)	0.186	-.060 - -.040	.667
PCS Magnify	0.306 (-0.05, 0.66)	0.181	.443 - .451	.091
PCS Helplessness	0.020 (-0.27, 0.31)	0.146	.258 - .307	.890

$R^2 = .60$

Note. PSS = Perceived Stress Scale; PCS = Pain Catastrophizing Scale

10.4.1.7 Hypothesis 2aiii - Results

Catastrophic negativity as a predictor of pain intensity ratings (in-patient and out-patient combined data sets).

Catastrophic negativity (a sub scale of the ADAPSS) as a single predictor did not significantly predict pain intensity ratings for in-patients T1 ($F(1, 58) = .066$, $p = .798$) or for out-patients ($F(1,45) = 1.456 - 1.879$, $p = .177 - .234$) when analysed using a linear regression model.

10.4.1.8 Hypothesis 2biii - Results

Catastrophic negativity as a predictor of life interference (out-patient data set).

Catastrophic negativity significantly predicted greater life interference from pain in a linear regression model, $F(1,45) = 35.55 - 44.04$, $p = 001$ and the model (Table 13) explained between 44.1% and 50.6% of variance.

Table 14. Linear model of catastrophic negativity as a predictor of life interference. 95% confidence intervals reported in parentheses.

	b	*SE B*	Beta	*p*
Constant	-13.582 (-26.50, -0.67)	6.590		.039
ADAPSS Catastrophic negativity	0.609 (0.42, 0.80)	0.098	.664 - .711	.001

$R^2 = .44 - .50$

Note. ADAPSS = Appraisals of Disability: Primary and Secondary Scale

10.4.1.9 Hypothesis 2ciii - Results

Catastrophic negativity as a predictor of pain-related distress (out-patient data set).

Catastrophic negativity was entered into a linear regression model to see if it predicted pain related distress. The model was significant, $F(1, 43) = 21.22 - 23.55$, $p = 001$, (Table 14) and explained between 30.5% and 32.9% of variance, indicating that an increase in catastrophic negativity predicted higher pain-related distress.

Table 15. Linear model of catastrophic negativity as a predictor of pain related distress. 95% confidence intervals reported in parentheses.

	b	*SE B*	Beta	*p*
Constant	-3.707 (-8.84, 1.42)	2.617		.157
ADAPSS Catastrophic negativity	0.185 (0.11, 0.26)	0.039	.566 - .586	.001

$R^2 = .30 - .33$
Note. ADAPSS = Appraisals of Disability: Primary and Secondary Scale

10.4.1.10 Hypothesis 2 - Summary of Results

In summary, mental defeat, anxiety and rumination did not contribute to the prediction of any of the three pain outcome measures. Higher perceived stress, depression and catastrophic negativity predicted increases in pain-related distress, and higher depression, pain magnification and catastrophic negativity predicted greater life interference from pain. Catastrophic thinking alone was predictive of increased reported pain intensity ratings, whereas lower pain intensity ratings were predicted by higher perceived stress.

10.4.2 Hypothesis 3 - Results

Positive psychological characteristics will predict pain intensity scores, the extent of life interference and levels of distress.

Forced entry multiple regression was used to analyse whether the positive psychological variables of resilience (a sub scale of the ADAPSS), activity engagement and pain willingness (sub scales of the CPAQ) would predict pain intensity ratings, the extent of life interference from pain and levels of pain related distress. In-patient T1 and out-patient samples were analysed separately where pain intensity is concerned as t-tests found a difference between the samples on the ADAPSS (resilience) and CPAQ (activity engagement and pain willingness) measures (see Hypothesis 1 results in Section 10.3).

10.4.2.1 Hypothesis 3a - Results

Activity engagement, pain willingness and resilience as predictors of pain intensity ratings (in-patient T1 and out-patient data sets analysed separately).

Positive psychological variables were not found to significantly predict pain intensity ratings for either the in-patient ($F(3,56) = 1.242$, $p = .303$) or out-patient ($F(3,43) = .271 - .452$, $p = .717 - .846$) groups when force entered into a regression model.

10.4.2.2 Hypothesis 3b - Results

Activity engagement, pain willingness and resilience as predictors of life interference (out-patient data set).

Resilience, activity engagement and pain willingness were force entered into a multiple regression model to see whether they predicted changes in life interference. The model (Table 15) showed a trend towards significance, F(3, 43) = 2.510 - 3.319, p = .029 - .071 and predicted between 14.9% and 18.8% of variance. Resilience was the only variable to significantly contribute towards predicting changes in life interference, suggesting that as resilience increases life interference reduces.

Table 16. Linear model of resilience, activity engagement and pain willingness as predictors of life interference. 95% confidence intervals reported in parentheses.

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	b	*SE B*	Beta	*p*
Constant	49.94 (29.29, 70.59)	10.53		.001
ADAPSS Resilience	-0.53 (-0.94, -0.12)	0.21	-.40 - -.34	.012
CPAQ Activity engagement	0.27 (-0.03, 0.56)	0.15	.25 - .31	.074
CPAQ Pain willingness	-0.25 (-0.56, 0.07)	0.16	-.28 - -.24	.129

R^2 = .14 - .18
Note: ADAPSS = Appraisals of Disability: Primary and Secondary Scale; CPAQ = Chronic Pain Acceptance Questionnaire.

10.4.2.3 Hypothesis 3c - Results

Activity engagement, pain willingness and resilience as predictors of pain-related distress (out-patient data set).

The prediction of pain-related distress was analysed using a regression model, whereby the three positive psychological variables were force entered. The model (Table 16) significantly predicted distress, $F(3,43) = 8.25 - 9.98$, $p < .001$, explaining between 32.7% and 36.9% of variance. Resilience and activity engagement were both significant predictors, with resilience predicting a decrease and activity engagement predicting an increase in pain-related distress.

Table 17. Linear model of resilience, activity engagement and pain willingness as predictors of pain-related distress. 95% confidence intervals reported in parentheses.

	b	*SE B*	Beta	*p*
Constant	23.35 (17.08, 29.62)	3.20		.001
ADAPSS Resilience	-0.32 (-0.44, -0.20)	0.06	-.65 - -.62	.001
CPAQ Activity engagement	0.09 (0.01, 0.19)	0.05	.28 - .31	.036
CPAQ Pain willingness	-0.08 (-0.18, 0.02)	0.05	-.23 - -.22	.108

$R^2 = .33 - .37$
Note: ADAPSS = Appraisals of Disability: Primary and Secondary Scale; CPAQ = Chronic Pain Acceptance Questionnaire.

10.4.2.4 Hypothesis 3 - Summary of Results

Where the positive psychological variables are concerned, greater resilience was predictive of less life interference from pain and lower pain-related distress, whereas higher activity engagement predicted greater distress. Neither resilience, activity engagement or pain willingness predicted pain intensity ratings. Pain willingness did not contribute to the prediction of any of the pain outcome measures.

10.4.3 Hypothesis 4 - Results

The way a significant other person responds to the individual in pain will predict pain intensity scores, the extent of life interference and levels of distress.

Forced entry multiple regression was used to analyse whether the response of a significant person to someone in pain would predict their pain intensity ratings, the extent of life interference from pain and their levels of pain-related distress. Responses, taken from the Multidimensional Pain Inventory, Section B, were classified as being distracting, negative or solicitous. In-patient T1 and out-patient samples for the outcome 'pain intensity' were analysed separately as *t*-tests found a difference between the samples on the solicitous responses (see Hypothesis 1 results in Section 10.3).

10.4.3.1 Hypothesis 4a - Results

Distracting, negative and solicitous responses as predictors of pain intensity ratings (in-patient T1 and out-patient data sets analysed separately)

The way a significant other person responded to the individuals expression of pain was not found to significantly predict pain intensity ratings for either the in-patient ($F(3, 56) = 0.23$, $p = .873$) or out-patient ($F(3, 43) = 0.86 - 1.00$, $p = .298 - .469$) groups when force entered into a regression model.

10.4.3.2 Hypothesis 4b - Results

Distracting, negative and solicitous responses as predictors of life interference (out-patient data set).

Distracting, negative and solicitous responses to pain expression were force entered into a multiple regression model to see whether they predicted life interference (Table 17). The model was significant, $F(3,43) = 6.52 - 8.10$, $p = .001$, explaining between 31.3% and 36.1% of variance. Distracting and negative responses significantly contributed to the model, suggesting that an increase in these type of responses to an individual in pain, predicts an increase in life interference from the pain.

Table 18. Linear model of distracting, negative and solicitous responses to an individual's pain as predictors of life interference. 95% confidence intervals reported in parentheses.

	b	*SE B*	Beta	*p*
Constant	14.18 (7.03, 21.33)	3.65		.001
Distracting	0.89 (0.20, 1.58)	0.35	.41 - .48	.012
Negative	1.40 (0.74, 2.05)	0.34	.52 - .57	.001
Solicitous	-0.33 (-0.94, 0.29)	0.31	-.22 - -.13	.297

$R^2 = .31 - .36$

10.4.3.3 Hypothesis 4c - Results

Distracting, negative and solicitous responses as predictors of pain-related distress (out-patient data set).

The way a significant other person responded to the individuals expression of pain was found to significantly predict pain-related distress, $F(3, 43) = 2.84 - 3.74$, $p = .018 - .049$, when distracting, negative and solicitous responses were force entered into a regression model (Table 18). The model explained between 16.5% and 20.7% of variance. Only negative responses were found to contribute significantly to the prediction of distress, indicating that as negative responses increased, distress could also be predicted to increase.

Table 19. Linear model of distracting, negative and solicitous responses to an individual's pain as predictors of pain-related distress. 95% confidence intervals reported in parentheses.

	b	*SE B*	Beta	*p*
Constant	5.90 (3.06, 8.73)	1.45		.001
Distracting	0.26 (-0.01, 0.53)	0.14	.33 - .39	.062
Negative	0.40 (0.14, 0.66)	0.13	.41 - .46	.003
Solicitous	-0.17 (-0.41, 0.07)	0.12	-.31 - -.22	.168

$R^2 = .17 - .21$

10.4.3.4 Hypothesis 4 - Summary of Results

Similarly to the previous hypothesis, none of the ways of responding to someone in pain predicted an individual's reported pain intensity ratings. Distracting and negative responses both predicted an increase in life interference and additionally, responding negatively predicted higher pain-related distress. Of particular note, and in contrast to research in the able-

bodied pain population, responding solicitously did not predict any of the pain-related oucomes, either in a positive or negative way.

10.4.4 Hypotheses 5ai, 5aii, and 5aiii - Results

Cortisol concentration levels will predict an increase in pain intensity scores, the extent of life interference and levels of distress.
Cortisol concentration levels were entered into a linear regression model to see whether this biological marker of stress would predict pain outcome measures. Cortisol did not significantly predict pain intensity (out-patient: $F(1,39) = 1.42$, $p = .241$; in-patient: $F(1,55) = 1.17$, $p = .285$) life interference ($F(1,39) = 0.28$, $p = .600$) or pain-related distress ($F(1,39) = .42$, $p = .520$), suggesting that it may not have a direct impact on pain-related outcomes.

10.5 Hypotheses 5bi, 5bii, 5biii, 5biv - Results

There will be a relationship between cortisol concentration levels and negative psychological variables, positive psychological variables, others responses and pain outcome variables.
The in-patient T3 and out-patient data sets were collapsed for these analyses as there were no differences found between them (see Hypothesis 1 results, Section 10.3). The cortisol data set was not normally distributed, it has outliers and tied ranks, therefore Kendall's tau was used to analyse the relationship between cortisol concentration levels and the other variables. As the data was not normally distributed, the missing data for this analysis was dealt with using expectation maximisation so that bootstrapping could be used.

Contrary to expectation, cortisol concentration level was not related to pain outcome measures on the MPI A scale (pain severity: $\tau = .136$, $p = .130$; pain-related distress: $\tau = .070$, $p = .436$; life interference: $\tau = .069$, $p = .436$), HADS depression, $\tau = .128$, $p = .069$ or HADS anxiety, $\tau = .095$, $p = .178$. It was significantly related to the total score of the PCS, $\tau = .183$, 95% BCa CI [.036, .313], $p = .008$, suggesting that as pain catastrophizing increases, so does cortisol concentration.

Each sub-scale of the PCS was then analysed to see which aspects of pain catastrophizing were associated with cortisol concentration. Helplessness, τ = .152, 95% BCa CI [.006, .289], p = .03, and rumination, τ = .236, 95% BCa CI [.102, .375], p = .001 were both positively correlated with cortisol concentration level but there was not a significant relationship with magnification, τ = .092, p = .202. As was anticipated, the PSS had a significant positive association with cortisol concentration, τ = .154, 95% BCa CI [-.004, .298], p = .027, as did a distracting response from a significant person, τ = .139, 95% BCa CI [-.005, .288], p = .047. However, it should be noted that the confidence intervals for both of these variables just cross zero, which suggests a non-significant result. Because the distribution of scores for cortisol are not normally distributed, and the bootstrap confidence intervals are less affected by this than the significance value, the confidence intervals should be considered a more reliable means from which to judge significance, and the *p*-value treated with caution.

10.5.1.1 Hypotheses 5b - Summary of Results

In summary, these results suggest that there is a positive relationship between cortisol concentration levels and pain catastrophizing. More specifically, as feelings of helplessness increase and people start to ruminate more about the pain, cortisol levels are raised. No other significant relationships were found.

10.6 **Hypothesis 6a - Results**

As in-patients adapt to their SCI, their biopsychosocial outcomes will collectively improve and stabilize.

One-way repeated-measures ANOVAs were carried out to compare in-patients scores on each measure at the three time points. Missing data was imputed using Expectation Maximisation. Mauchly's Test of sphericity assumed sphericity in each of the results reported below. There was a significant effect of time on the ADAPSS resilience scale, $F(2, 56) = 9.49$, $p < .001$, partial $\eta^2 = .25$, indicating that resilience to SCI declined over time, however this represents a small effect size. Pairwise comparisons (Figure 22) indicate that there were significant differences between T1 ($M = 54.00$, $SD = 11.44$) and T2 ($M = 47.93$, $SD = 11.97$), $p = .013$, and T1 and T3 ($M = 47.18$, $SD = 10.61$), $p < .001$.

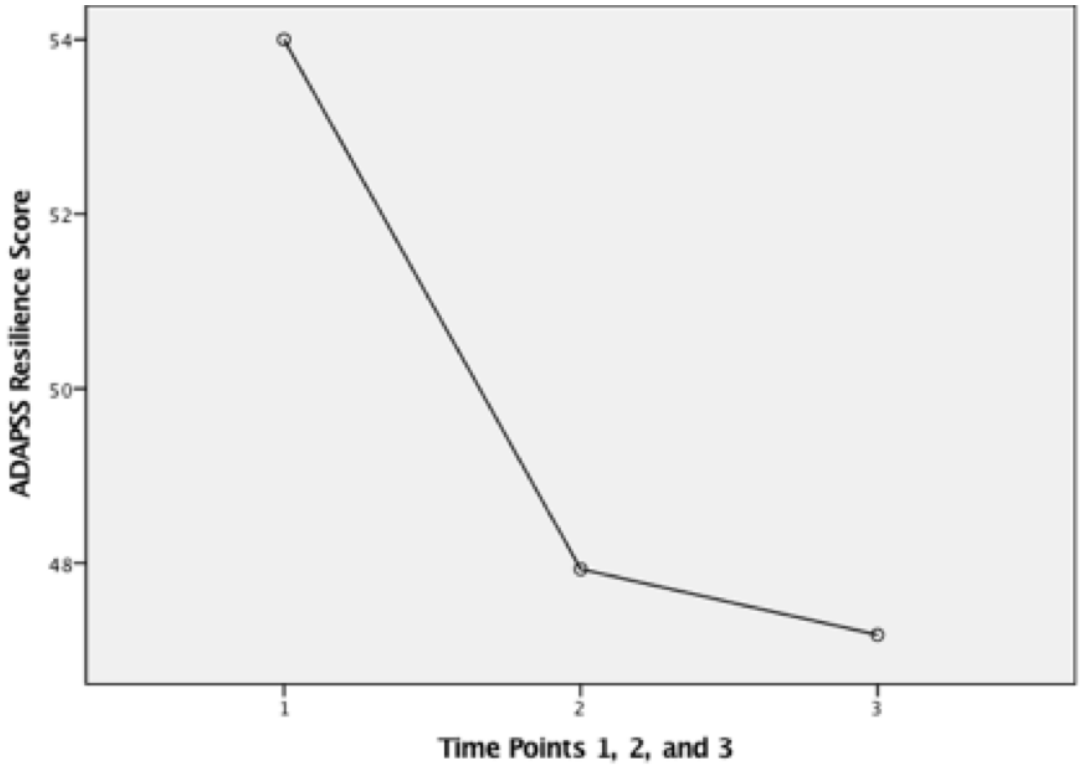


Figure 22. Difference in means across three time points – ADAPSS resilience scale. ADAPSS = Appraisal of Disability Primary and Secondary Scale.

There was also a significant effect of time on the HADS depression scale, $F(2, 56) = 3.96$, $p = .025$, partial $\eta^2 = .12$ suggesting that over time, depression scores increased. This represents a small effect size. Pairwise comparisons (Figure 23) show a significant difference between T1 ($M = 9.48$, $SD = 4.06$) and T3 ($M = 12.72$, $SD = 4.72$), $p = .012$, with scores at T3 higher than at T1.

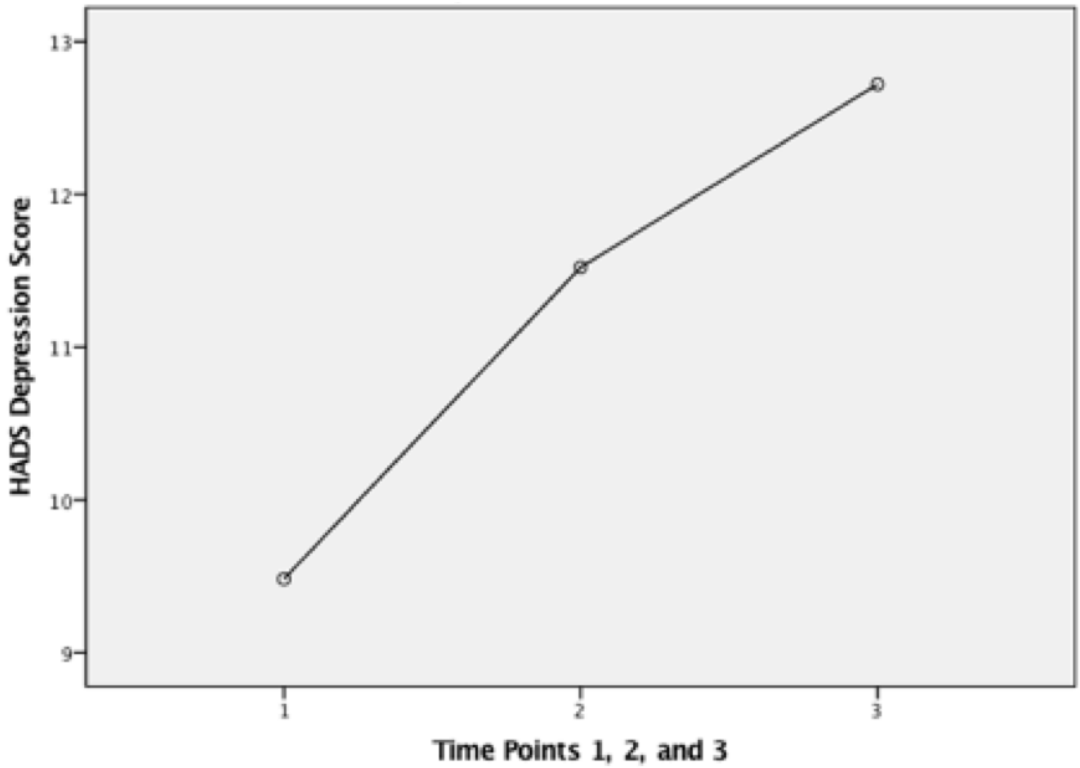


Figure 23. Difference in means across three time points – HADS depression scale. HADS = Hospital Anxiety and Depression Scale.

The only other significant effect was between time and the magnification sub-scale of the PCS, $F(2, 56) = 4.118$, $p = .021$, partial $\eta^2 = .13$, representing a small effect size. Pairwise comparisons (Figure 24) show a significant difference between T1 ($M = 3.41$, $SD = 2.96$) and T2 ($M = 5.18$, $SD = 3.13$), $p = .053$. The mean score for T3 ($M = 4.53$, $SD = 2.60$) was higher than T1 but lower than T2, but these differences were not significant, suggesting that the tendency to magnify the experience of pain increases initially but then starts to reduce again. No significant effects were found on any of the other variables

across the different time points.

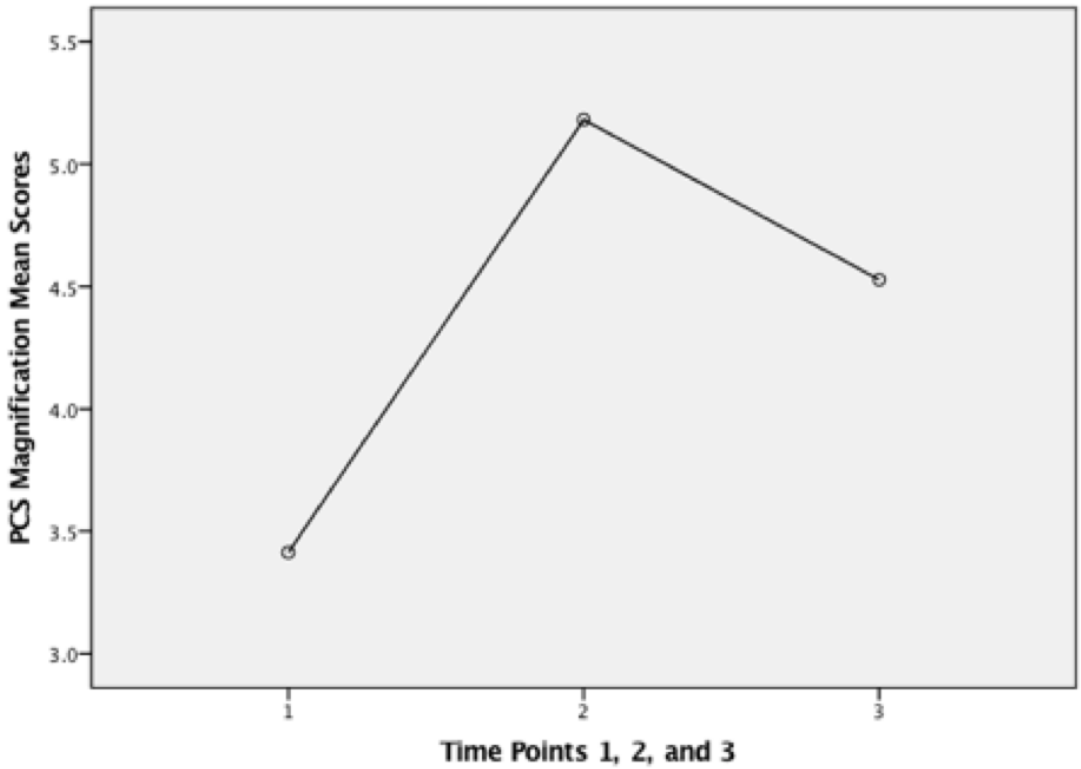


Figure 24. Difference in means across three time points – PCS Magnification.
PCS = Pain Catastrophizing Scale

10.6.1.1 Hypothesis 6a - Summary of Results

Across the three time-points psychological wellbeing of the in-patient sample declined, with depression and magnification of pain both increasing. Additionally, participants showed reduced resilience to their SCI over the nine month period.

10.7 **Hypothesis 6b - Results**

There will be a relationship between time since injury and each variable.
The in-patient T1 and out-patient data sets were individually used to analyse the relationship between 'time since injury' and catastrophic negativity (ADAPSS), resilience (ADAPSS), solicitous responses (MPIb), pain acceptance (CPAQ total score) and activity engagement (CPAQ subscale).

These two data sets were collapsed to analyse the relationship between ‘time since injury’ and each of the other variables because no differences were found between them (see Hypothesis 1 results, Section 10.3). Expectation Maximisation was used to impute missing data. The ‘time since injury’ data was not normally distributed so Spearman’s Rho was used to analyse the relationship between that and each variable.

Time since injury was positively associated with mental defeat, r = .192, 95% BCa CI [.006, .384], p = .047, and with the helplessness subscale of the PCS, r = .249, 95% BCa CI [.070, .424], p = .010, suggesting that the longer it has been since an individuals injury, the more likely they are to feel helpless and experience mental defeat. Time since injury was negatively associated with receiving a distracting response from a significant other person, r = -.196, 95% BCa CI [-.389, .019], p = .043, although the confidence intervals cross zero so the p-value should be treated with caution. The confidence intervals are less affected than the p-values by data which does not have a normal distribution, so it can be considered that this relationship is not significant. There was also a negative association with cortisol concentration levels, r = -.344, 95% BCa CI [-.529, -.130], p = .001, suggesting that over time, cortisol concentration levels decrease.

10.7.1.1 Hypothesis 6b - Summary of Results

In accordance with Hypothesis 6, the results suggest that over time psychological well-being declines, with increases in helplessness (related to catastrophic thinking) and mental defeat. Cortisol concentration levels reduce with the passing of time. Time since injury was not significantly correlated with any other variables.

10.8 Results - Stage 2 Analysis

10.8.1 Mediation Analysis

The literature reviewed suggests that some of the variables included in this study may be either predictors of pain-related outcomes or mediators between biopsychosocial variables and the consequences of pain. It has been suggested that pain catastrophizing (Furrer, Michel, Terrill, Jensen, & Müller, 2019), and pain acceptance (Pinto-Gouveia, Costa, & Marôco, 2016) might both be important mediators and exert their influence on pain-related outcomes through mediating the effects of various psychosocial variables. There is evidence to suggest that cognitive appraisal of injury mediates the relationship between stress and depression (Catalano, Chan, Wilson, Chiu & Muller, 2011), but studies have not explored whether appraisal of injury might have a broader role as a mediator where pain is concerned, and provide the bridge between SCI and pain. As few studies have attempted to identify mediators between biopsychosocial variables and pain outcomes in SCI, the second stage of analysis in this study explores whether pain catastrophizing, pain acceptance and appraisal of injury might emerge to have an important mediating role in pain conditions for people with SCI. Additionally, because stress and cortisol are so closely associated each one was used as both predictor and mediator of the other on pain outcomes.

Mediation analysis investigates whether there is an indirect effect of a predictor variable (X) on an outcome variable (Y) via one or more mediators (M), therefore explaining why the relationship exists. This mediation model is shown in Figure 25. Path *c* represents the total effect of the predictor (X) on the outcome (Y) ignoring any mediators (M). Path *c* also represents the direct effect of the predictor on the outcome when the mediator is included in the model, often denoted as c^1. Path *a* represents the effect of the predictor on the mediator and path *b* represents the effect of the mediator on the outcome. A mediated or indirect effect of the predictor on the outcome is the product of the *a* and *b* paths, often represented as *a*b* or *a* x *b.* Baron and Kenny (1986) proposed that for mediation to occur the predictor must have a statistically

significant effect on both the outcome (the total effect) and on the mediator and that the mediator must have a statistically significant effect on the outcome. However, it has now been established that this is not the case and that mediation can occur where there is not a statistically significant total effect (Zhao, Lynch & Chen, 2010).

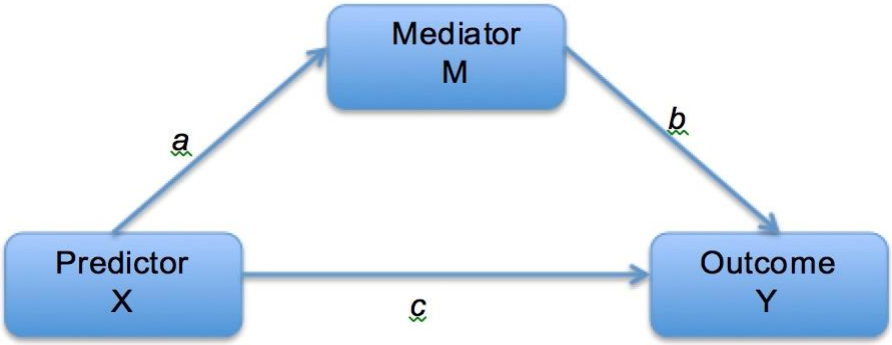


Figure 25. A Three-Variable Causal Mediation Model

Figure 26 shows the different patterns of mediation or non-mediation that can occur. The top half of the diagram demonstrates how data can lead to three patterns of mediation and two patterns of non-mediation. On the far left, complementary mediation occurs when there is a direct effect (the effect of the predictor on the outcome when the mediator is included in the model, path c^1) and an indirect effect (the effect of the predictor on the outcome via one or more mediators) pointing in the same direction. Competitive mediation (2nd from left) occurs when there are significant indirect and direct effects but in opposite directions. The final pattern of mediation is an indirect-only mediation where no direct effect occurs. Non-mediation can be inferred when there is only a direct effect but no indirect effect and when there are no significant effects of any kind. The bottom half of the table shows how these different patterns of mediation can be interpreted. In complementary mediation, competitive mediation and direct-only non-mediation it is likely that other mediators exist that have not been included in the model. Further exploratory research may need to be carried out to identify these. Where there is an

indirect-only mediation it suggests the theoretical framework being tested is robust and it is unlikely that another mediator might be involved. If there are no significant effects at all it suggests that the theoretical framework is incorrect. The results of this mediation analysis will be reported, and later discussed, in line with this diagram.

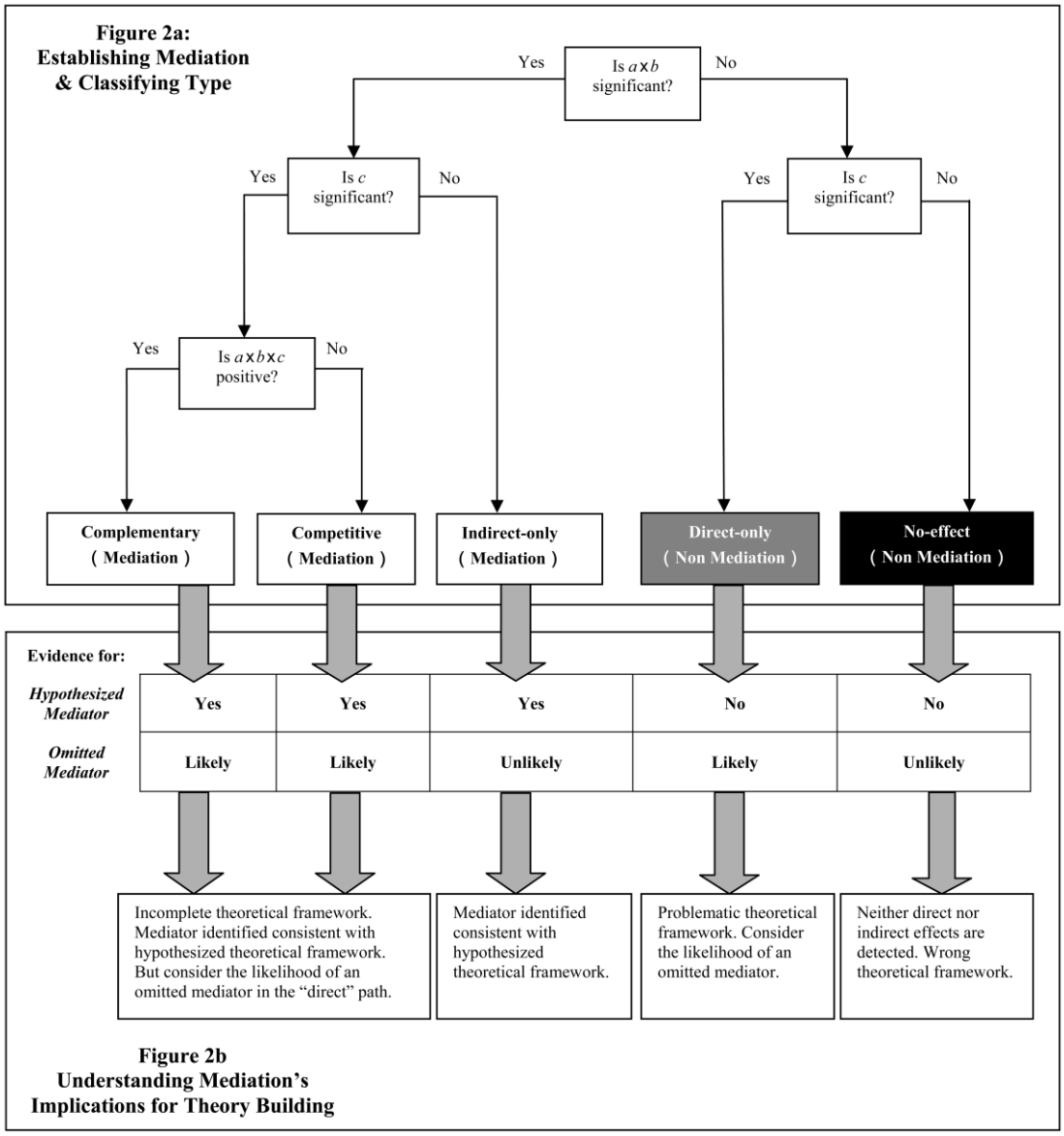


Figure 26. Decision Tree for Establishing and Understanding Types of Mediation and Non-mediation. See text for full description. From "Reconsidering Baron and Kenny: Myths and truths about mediation analysis," by X. Zhao, J. G. Lynch, and Q. Chen, 2010, *Journal of Consumer Research, 37*, p. 201. Copyright 2010 by Journal of Consumer Research.

The in-patient T3 and out-patient datasets combined were used for all analyses except those involving depression as a significant difference was found between out-patients and in-patients T3 on this variable (see Hypothesis 1 results, Section 10.3). The out-patient dataset alone was used for all of the analyses that included depression. The effect of each variable on the LANSS pain intensity rating, the Multidimensional Pain Inventory section A (MPIA) pain outcomes of life interference, distress, support and life control, and the Multidimensional Pain Inventory section C (MPIC) outcomes of activity level (MPICa) and degree to which activity has been reduced by pain (MPICb) were analysed with four different mediators: pain catastrophizing; pain acceptance; and the ADAPSS sub scales catastrophic negativity and resilience. A full summary of significant results are shown in Tables 19-21 below. The significant statistical results showing the beta values, *p*-values and confidence intervals can be found in Appendix 3 Mediation Analysis Statistical Results. All confidence intervals for the indirect effects are BCa bootstrapped CI's based on 5000 samples, and in mediation analysis these are used to assess the significance of the indirect result rather than a *p*-value. Expectation Maximisation was used to impute missing data.

Table 20. Mediation Analysis Summary With Pain Catastrophizing (PCS) as the Mediator.

Predictor	Outcome	Direct Effect	Total Effect	Indirect Effect	Data Set
Cortisol	Pain Intensity			✓	T3 + Out
	Life Interference			✓	
	Distress			✓	
	Life Control			✓	
	MPICb			✓	
Depression	Pain Intensity			✓	Out
	Life Interference	✓	✓		
	Distress	✓	✓		
	Life Control	✓	✓		
	MPICb			✓	
ADAPSS Negativity	Pain Intensity			✓	T3 + Out
	Life Interference	✓	✓		
	Distress	✓	✓		
	Life Control	✓	✓		
	MPICa		✓		
	MPICb	✓	✓		
ADAPSS Resilience	Pain Intensity			✓	T3 + Out
	Life Interference		✓	✓	
	Distress	✓	✓	✓	
	Support	✓	✓		
	Life Control	✓	✓	✓	
	MPICa	✓	✓		
	MPICb			✓	
Acceptance	Pain Intensity	✓		✓	T3 + Out
	Life Interference			✓	
	Distress			✓	
	Support	✓	✓		
	Life Control			✓	
	MPICb			✓	
Anxiety	MPICb		✓	✓	T3 + Out
	Pain Intensity			✓	
	Life Interference	✓	✓	✓	
	Distress	✓	✓	✓	
	Life Control	✓	✓	✓	
Negative Response	Life Interference	✓	✓		T3 + Out
	Distress	✓	✓		T3 + Out
Distracting Response	Support	✓	✓		T3 + Out
Solicitous Response	Support	✓	✓		T3 + Out

Predictor	Outcome	Direct Effect	Total Effect	Indirect Effect	Data Set
Mental Defeat	Pain Intensity		✓		T3 + Out
	Life Interference		✓	✓	
	Distress		✓		
	Life Control		✓		
	MPICb			✓	
Stress	Pain Intensity			✓	T3 + Out
	Life Interference		✓	✓	
	Distress	✓	✓		
	Life Control	✓	✓	✓	
	MPICb			✓	

Note. Total Effect = Effect of predictor on outcome when mediator is not present in the model (Path c). Direct Effect = Effect of predictor on outcome when mediator is in the model – regression of outcome predicted from both predictor and mediator (mediator treated as predictor). Indirect effect = Effect of predictor on outcome via mediator. MPICa = Multidimensional Pain Inventory section C activity level; MPICb = Multidimensional Pain Inventory section C degree to which activities reduced by pain.

Table 21. Mediation Analysis Summary With Pain Acceptance as the Mediator.

Predictor	Outcome	Direct Effect	Total Effect	Indirect Effect	Data Set
Negative Response	Life Interference	✓	✓		T3 + Out
	Distress	✓	✓		
Distracting Response	Support	✓	✓		T3 + Out
Solicitous Response	Support	✓	✓		T3 + Out
Pain Catastrophizing	Pain Intensity	✓	✓		T3 + Out
	Life Interference	✓	✓		
	Distress	✓	✓		
	Support			✓	
	Life Control	✓	✓		
	MPICb	✓	✓		
ADAPSS Negativity	Life Interference	✓	✓		T3 + Out
	Distress	✓	✓		
	Life Control	✓	✓		
	MPICa		✓		
	MPICb	✓	✓		
ADAPSS Resilience	Life Interference	✓	✓		T3 + Out
	Distress	✓	✓		
	Support		✓		
	Life Control	✓	✓		
	MPICa	✓	✓		
Mental Defeat	Pain Intensity	✓	✓		T3 + Out
	Life Interference	✓	✓		
	Distress	✓	✓		
	Support			✓	
	Life Control	✓	✓		
Anxiety	Life Interference	✓	✓		T3 + Out
	Distress	✓	✓		
	Life Control	✓	✓		
	MPICb	✓	✓		
Stress	Life Interference	✓	✓		T3 + Out
	Distress	✓	✓		
	Support			✓	
	Life Control	✓	✓		
Depression	Life Interference	✓	✓		Out
	Distress	✓	✓		
	Life Control	✓	✓		
	MPICb	✓			

Note. Total Effect = Effect of predictor on outcome when mediator is not present in the model (Path c). Direct Effect = Effect of predictor on outcome when mediator is in the model – regression of outcome predicted from both predictor and mediator (mediator treated as predictor). Indirect effect = Effect of predictor on outcome via mediator. MPICa = Multidimensional Pain Inventory section C activity level; MPICb = Multidimensional Pain Inventory section C degree to which activities reduced by pain.

Table 22. Mediation Analysis Summary With ADAPSS Catastrophic Negativity and Determined Resilience as the Mediators.

Predictor	Outcome	Direct Effect	Total Effect	Indirect Effect			Data Set
				Tot	Neg	Res	
Mental Defeat	Pain Intensity	✓	✓				T3 + Out
	Life Interference		✓	✓	✓		
	Distress		✓	✓	✓	✓	
	Life Control		✓	✓	✓	✓	
	MPICa			✓		✓	
	MPICb			✓	✓		
Stress	Life Interference		✓	✓	✓		T3 + Out
	Distress	✓	✓	✓			
	Support					✓	
	Life Control		✓	✓	✓	✓	
	MPICa			✓		✓	
	MPICb			✓	✓		
Distracting Response	Life Interference	✓					T3 + Out
	Distress					✓	
	Support	✓	✓				
	Life Control					✓	
	MPICa					✓	
Negative Response	Life Interference	✓	✓	✓	✓		T3 + Out
	Distress		✓	✓	✓	✓	
	Support					✓	
	Control			✓	✓	✓	
	MPICa			✓		✓	
	MPICb				✓		
Solicitous Response	Support	✓	✓				T3 + Out
Pain Catastrophizing	Pain	✓	✓				T3 + Out
	Life Interference		✓	✓	✓		
	Distress		✓	✓	✓	✓	
	Support					✓	
	Life Control		✓	✓	✓	✓	
	MPICa					✓	
	MPICb		✓		✓		
Acceptance	Distress			✓		✓	T3 + Out
	Support	✓	✓				
	Life Control			✓		✓	
	MPICa			✓		✓	

Predictor	Outcome	Direct Effect	Total Effect	Indirect Effect			Data Set
				Tot	Neg	Res	
Anxiety	Life Interference	✓	✓	✓	✓		T3 + Out
	Distress	✓	✓	✓		✓	
	Support					✓	
	Life Control	✓	✓	✓	✓	✓	
	MPICa					✓	
	MPICb		✓	✓	✓		
Depression	Life Interference	✓	✓	✓	✓		Out
	Distress	✓	✓	✓		✓	
	Support				✓	✓	
	Control		✓	✓	✓		
	MPICa					✓	

Note. Total Effect = Effect of predictor on outcome when mediator is not present in the model (Path c). Direct Effect = Effect of predictor on outcome when mediator is in the model – regression of outcome predicted from both predictor and mediator (mediator treated as predictor). Indirect effect = Effect of predictor on outcome via mediator. MPICa = Multidimensional Pain Inventory section C activity level; MPICb = Multidimensional Pain Inventory section C degree to which activities reduced by pain. Tot = total effect; Neg = Catastrophic Negativity; Res = Determined Resilience.

10.8.1.1 Pain Catastrophizing as the Mediator

The mediation analysis demonstrated the importance of pain catastrophizing as a mediator between many of the predictor variables and pain outcomes. The model is shown in Figure 27. This was particularly the case for the predictors Cortisol, ADAPSS resilience, pain acceptance, anxiety and stress, where catastrophizing mediated the effect on between four and five pain outcomes (pain intensity, life interference, life control, distress, and MPICb). It also mediated the effect between depression and two pain outcomes, (pain intensity and MPICb), and mental defeat and two pain outcomes, (life interference and MPICb), and between ADAPSS negativity and pain intensity. Pain catastrophizing did not mediate the effect of others' responses on pain outcomes.

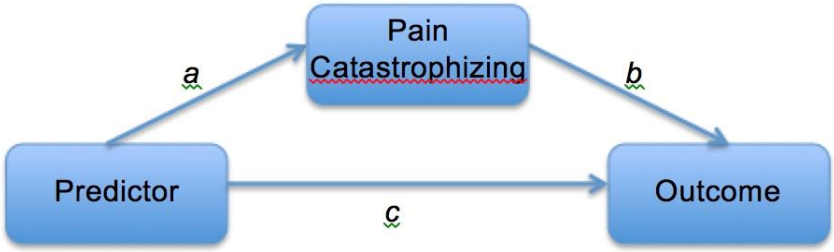


Figure 27. Mediation Model with Pain Catastrophizing as the Mediator

Much research has associated cortisol levels with depression. However, as cortisol was not related to depression in the earlier reported analysis (section 10.5), and as pain catastrophizing was a strong mediator between many of the psychological variables and pain outcomes, a further exploratory analysis was undertaken with cortisol concentration level as the predictor, pain catastrophizing as the mediator and depression as the outcome. Cortisol did not directly affect depression scores but there was an indirect effect suggesting that higher cortisol concentration affects depression when pain catastrophizing is also high.

10.8.1.2 Pain Acceptance as the Mediator

Figure 28 shows the mediation model with acceptance as the mediator. Pain acceptance was not a significant mediator, only mediating the effects of pain catastrophizing, mental defeat and stress on the single pain outcome of support. There were significant total and direct effects between many of the predictor variables and pain outcomes however, suggesting that other mediators may be important such as pain catastrophizing.

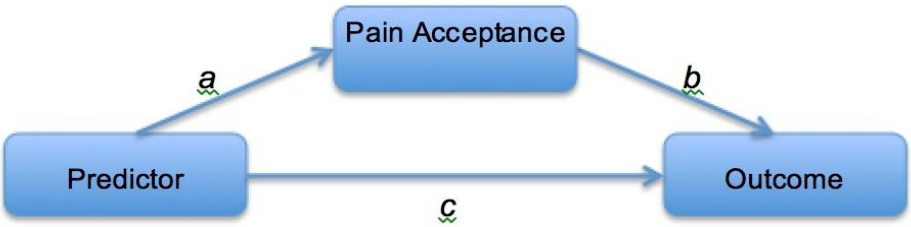


Figure 28. Mediation Model With Pain Acceptance as the Mediator.

10.8.1.3 Catastrophic Negativity and Determined Resilience as Mediators

The third set of analyses examined whether the subscales of the ADAPSS (catastrophic negativity and resilience) had a mediating effect on pain outcomes (Figure 29). The way people appraised their disability had a strong mediating effect between all the predictor variables (apart from cortisol and solicitous response from a significant other person) and many of the pain outcomes (pain intensity, life interference, life control, distress, and MPICb). This was the case for the total model with both subscales entered as mediators, and for each subscale individually. This has important implications for people with a SCI as it links appraisal of injury with key pain outcomes, suggesting another way in which appraisal of disability might impact on adjustment to SCI.

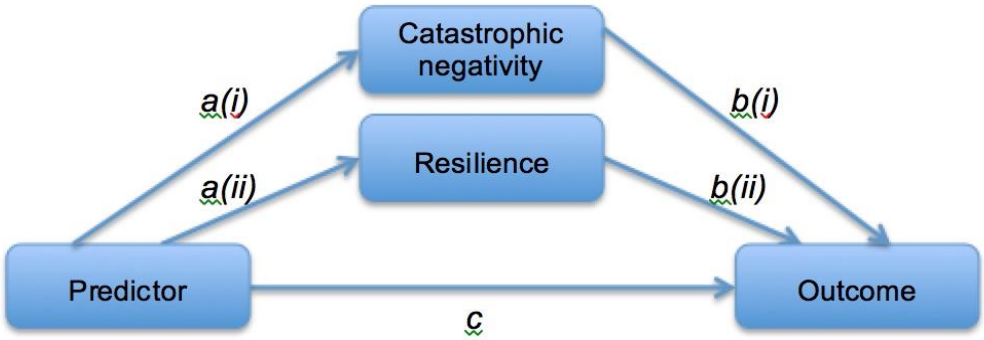


Figure 29. Mediation Model With Catastrophic Negativity and Resilience as the Mediators.

Because of the close association between stress and cortisol, each was used as predictor and mediator on each of the pain outcomes. There were no significant indirect effects of stress on the pain outcomes when cortisol was included as mediator or of cortisol on the pain outcomes when stress was included as a mediator.

10.8.2 **Regression Analysis on ADAPSS**

It was noted that many of the predictor variables in the mediation analysis had a significant effect on both of the ADAPSS subscales. As the way an individual appraises their disability is important with regards to how well they adapt to it (Chevalier, Kennedy & Sherlock, 2009), regression analysis was carried out to see whether psychological and social variables predicted the type of appraisals made. In-patient T3 and out-patient data sets were combined for this analysis as earlier tests had shown no differences between them on the measures used except one (see Hypothesis 1 results Section 10.3). Depression was not included in the analysis because there were significant differences between the two data sets on that subscale of the HADS. Missing data was imputed using Expectation Maximisation. A summary of the results can be seen in Table 22 below. Detailed results of the analysis are then provided.

Table 23. Summary of the Stage 2 multiple regression analysis results

Predictor	Catastrophic negativity	Resilience
Catastrophizing	+	0
Mental Defeat	+	0
Pain Acceptance	0	+
Anxiety	+	0
Perceived Stress	0	-
Distracting Response	0	+
Negative Response	0	-
Solicitous Response	0	0

Note. - = negative relationship; + = positive relationship; 0 = no relationship

Forced entry multiple regression was used to analyse whether stress, pain acceptance, anxiety, pain catastrophizing and mental defeat would predict ratings on the catastrophic negativity sub scale of the ADAPSS. The model (Table 23) was significant, $F(5, 70) = 25.17$, $p < 001$, explaining 64.3% of variance. Anxiety, pain catastrophizing and mental defeat were all significant predictors, with higher scores in each predicting an increase in catastrophic negativity.

Table 24. Linear model of psychological predictors of catastrophic negativity. 95% bias corrected and accelerated confidence intervals reported in parentheses. Confidence intervals and standard errors based on 1000 bootstrap samples.

	b	*SE B*	Beta	*p*
Constant	42.66 (34.71, 52.43)	4.87		.001
PCS	0.31 (0.01, 0.55)	0.15	.30	.033
PSPS	0.155 (0.04, 0.31)	0.064	.32	.026
CPAQ	-0.01 (-0.12, 0.08)	0.05	-.02	.783
HADS Anxiety	0.56 (0.18, 0.94)	0.18	.21	.005
PSS	0.24 (-0.13, 0.58)	0.18	.14	.186

$R^2 = .64$
PCS = Pain Catastrophizing Scale; PSPS = Pain Self-Perception Scale; CPAQ = Chronic Pain acceptance Questionnaire; HADS = Hospital Anxiety and Depression Scale; PSS = Perceived Stress Scale.

The same predictors were regressed onto the determined resilience subscale of the ADAPSS. This model (Table 24) was also significant, $F(5, 70) = 12.78$, $p = <.001$, and explained 48% of the variance. Pain acceptance and perceived stress were both significant predictors with pain acceptance predicting an increase in resilience and perceived stress predicting a decrease.

Table 25. Linear model of psychological predictors of resilience. 95% bias corrected and accelerated confidence intervals reported in parentheses. Confidence intervals and standard errors based on 1000 bootstrap samples.

	b	*SE B*	Beta	*p*
Constant	60.90 (52.19, 67.31)	4.13		.001
PCS	0.04 (-0.16, 0.24)	0.10	.06	.642
PSPS	-0.05 (-0.16, 0.04)	0.05	-.15	.324
CPAQ	0.08 (0.01, 0.18)	0.04	.20	.052
HADS Anxiety	-0.14 (-0.47, 0.26)	0.18	-.07	.440
PSS	-0.68 (-1.04, -0.32)	0.17	-.52	.001

$R^2 = .48$
PCS = Pain Catastrophizing Scale; PSPS = Pain Self-Perception Scale; CPAQ = Chronic Pain acceptance Questionnaire; HADS = Hospital Anxiety and Depression Scale; PSS = Perceived Stress Scale.

Distracting, negative and solicitous responses to pain expression were force entered into a multiple regression model to see whether they predicted scores on the catastrophic negativity and resilience sub scales of the ADAPSS. They did not predict catastrophic negativity, $F(3,72) = 1.31$, $p = .279$, but where

resilience was concerned the model (Table 25) was significant, $F(3,72) = 5.91$, $p = .001$, explaining 20% of variance. Distracting responses gave a significant positive contribution to the model suggesting that an increase in distracting responses when an individual is in pain predicts an increase in resilience. Negative responses gave a significant negative contribution to the model, suggesting that an increase in this type of response predicts a decrease in resilience.

Table 26. Linear model of distracting, negative and solicitous responses to an individual's pain as predictors of resilience. 95% bias corrected and accelerated confidence intervals reported in parentheses. Confidence intervals and standard errors based on 1000 bootstrap samples.

	b	*SE B*	Beta	*p*
Constant	47.64 (42.97, 53.29)	2.52		.001
Distracting	0.52 (0.05, 0.93)	0.23	.31	.025
Negative	-0.52 (-0.89, -0.23)	0.17	-.33	.002
Solicitous	-0.03 (-0.32, 0.31)	0.16	-.03	.828

$R^2 = .20$

10.8.2.1 Regression analysis on ADAPSS - Summary of results

In summary, increases in anxiety, catastrophic thinking and mental defeat all predicted a more catastrophic and negative way of appraising SCI. Higher stress and negative responses from a significant other person predicted lower resilience. In contrast, greater acceptance of pain and more distracting responses predicted increased resilience with regards to SCI.

11 Chapter 9 - Discussion

The aim of this research was to examine the biopsychosocial variables associated with pain in people with a SCI. A cross-sectional, repeated measures study was undertaken with out-patients of the NSIC and SIA, who had been discharged from hospital for a minimum of two years. A longitudinal, multiple-assessment point study was carried out with in-patients of the NSIC. All participants completed pain-related questionnaires measuring symptoms of neuropathic pain, pain intensity, degree of activity engagement, the degree to which pain reduced activity engagement, and the pain-related outcomes of distress, life interference, life control and support. Six psychological questionnaires measured perceived stress, pain catastrophizing, appraisal of disability, anxiety and depression, mental defeat and pain acceptance. The way a significant other responded to the individual's pain was assessed in terms of whether they tended to give distracting, negative or solicitous responses. Additionally, cortisol concentration level was analysed to see how this interacted with the other variables. In-patient participants completed these assessments on three occasions: time one (T1), when participants were in hospital, were identified as meeting the research criteria, and considered well-enough to participate, time two (T2) which occurred six months after the first time point, and time three (T3) which occurred nine months after the first time point, by which time the majority of participants had been discharged.

11.1 Comparison of in-patient and out-patient participants.

The first hypothesis predicted a difference between in-patient participants at the first measurement point (T1) and out-patient participants, and between in-patients at the third time point (T3) and out-patients, in each of the variables measured. There were no significant differences between in-patients at time one and out-patients with regards to their reported pain intensity, mood, anxiety, perceived stress, catastrophic thinking and the degree to which they experienced mental defeat in relation to their pain, which does not fully support hypothesis one. Although there is little research examining the differences

between in-patients and out-patients on these variables, it might have been expected that these factors would have been lower in out-patients than in-patients as the out-patient participants have had longer to adjust to their injury. As there were no differences between the two groups it suggests that these variables do not change over time for people who have both pain and a SCI. These variables could therefore be more trait-like, which would indicate that personality may be important in adjustment to SCI. This would support the literature in health psychology more broadly, which associates the Big Five personality factors (openness to experience, conscientiousness, extraversion, agreeableness, and neuroticism; McCrae & Costa, 1987) with the risk of disease and mental wellbeing (Weston, Hill & Jackson, 2015). For example, conscientiousness and openness predict a lower risk of contracting a disease (Weston et al., 2015) and are associated with better mental wellbeing whilst neuroticism represents a higher risk factor for disease and is associated with poorer mental health (Arieli, Kim & Martin, 2018).

In SCI, personality factors have been found to predict long-term adjustment to injury (Krause & Rohe, 1998), with high emotional lability considered a risk factor for poorer adaptive outcomes (Masten & Reed, 2005) and a positive temperament associated with positive adaptive outcomes (Catalano, Chan, Wilson, Chiu, & Miller, 2011). Whether mood, anxiety, perceived stress, pain catastrophizing and mental defeat are associated with personality factors has not been explored in this study and therefore requires further research. Additionally, whether they are higher in general in people with SCI than in the able bodied population cannot be assumed from this study, although previous research suggests that this is the case where depression and anxiety are concerned (Kennedy & Rogers, 2000; Ullrich, Jensen, Loeser & Cardenas, 2007; Battalio, Glette, Alschuler, & Jensen, 2018). This is of concern because, taken together with these results, it implies that psychological distress is high during rehabilitation and remains so after transition to the community for people with SCI and pain. As depression, anxiety and pain catastrophizing are known to interfere with rehabilitation goals (Tran, Dorstyn & Burke, 2016; Craig, Guest, Tran, Nicholson Perry & Middleton, 2017), on-going difficulties with adjustment and functioning may therefore, continue to be experienced. If

personality variables might be exacerbating such difficulties, this needs to be considered during rehabilitation.

11.1.1 Comparison of in-patients T1 and T3 and out-patients in pain acceptance

Where pain acceptance is concerned, the sub scales of The CPAQ (McCracken, Vowles & Eccleston, 2004), activity engagement and pain willingness, were analysed separately. In-patients at time one showed significantly higher acceptance of their pain than out-patients and this was demonstrated through greater engagement in activities. This implies that it might be easier to be accepting of pain and to engage in activities despite the pain in a hospital environment where activities are organised for individuals and undertaken with the support of health professionals. At the third time point, the difference in pain acceptance between the in-patient and out-patient groups was no longer present. All but two of the in-patient group had left hospital by this time supporting the idea that greater pain acceptance through activity engagement was more achievable when people had professional support and scheduled activities that were designed to improve their condition.

Whilst in hospital there is a requirement for spinal patients to engage with rehabilitation activities such as physiotherapy and occupational therapy (New et al., 2012), and it is more difficult to decline to do these as they represent a road to improvement, which might be a valued goal. Once out of hospital, health professionals are not always present to suggest that activity engagement will continue to lead to improvements in mobility and functioning (van Loo, Post, Bloemen, & van Asbeck, 2010; Whalley Hammell, 2007). Additionally, the health professionals that are seen in the community often do not have the specialist knowledge required to guide on-going rehabilitation (Cox, Amsters, & Pershouse, 2001; Neri & Kroll, 2003). Therefore, with the presence of pain there may be less motivation to engage in activities, as engagement results in increased pain. This supports the idea that individuals may be less sensitive to pain when pursuing valued goals (Van Damme, Legrain, Vogt, & Crombez, 2010), and that if the goal is valued highly people

will be more likely to persist in their efforts to achieve it regardless of the pain (Crombez et al. 2012). The MPM of pain (Eccleston & Crombez, 2007; see section 6.3 for a full description of this model) suggests that people become stuck in a perseverance loop when attempts to remove or reduce pain repeatedly fail, causing continuing worry and distress. Once out of hospital, this study suggests that on-going pain interferes with achieving important goals, leading the individual to engage in repeated attempts to solve the problem of pain. The most highly valued goal then becomes the removal of pain, resulting in lower pain acceptance and increasing the possibility of getting stuck in a loop of pain problem solving perseverance (Hearn, Cotter, Fine & Finlay, 2015).

Similarly, the Hexaflex Model of acceptance (Hayes, Strosahl & Wilson, 2012) also emphasises the importance of goal achievement but through psychological flexibility (see Section 6.4.2 for a full description). This suggests that psychological flexibility results from being able to stay in the present moment without focusing on the past or the future, identifying what is of value so that this can inform choices and decisions, deciding on the actions that need to be taken and being persistent but flexible in carrying them out, and observing thoughts and feelings whilst recognising that they are not facts (Hayes, Strosahl & Wilson, 2012). It defines acceptance in terms of an individual's willingness to engage in the pursuit of valued goals in the presence of unpleasant sensations and cognitions (Hayes et al., 2012).

This model might be appropriate in the able-bodied population but less relevant to people with a SCI. The results of this study suggest that willingness to engage in valued goals in the presence of pain declines when people are back in the community and facing the challenges that accompany this. For people with SCI, the goals of independence can be difficult to achieve in the presence of pain (Gruener, Zeilig, Laufer, Blumen & Defrin, 2018). Being persistent, yet flexible, in pursuing such goals is less realistic because there are some tasks of daily living (for example, transferral from a wheelchair) that require much more effort, and yet are necessary, for some people confined to a wheelchair. Taking an accommodative strategy therefore, described by Van

Damme, Crombez and Eccleston, (2008) as disengaging from unattainable goals and engaging in new ones, is not always possible, as the goals that seem unattainable might be the ones that are most important to persevere with in order to live an independent life. Therefore, the removal or reduction of pain is seen as being imperative if independence is to be achieved.

Additionally another facet of acceptance, staying in the present moment of pain, may be far less adaptive than looking forward to a future with greater independence because remaining in the present moment may lead to greater distress, as suggested by this study, rather than less distress. In contrast, focusing on and maintaining hope in the future may result in greater resilience and openness to new experiences (Sparkes & Smith, 2008). This is in line with Dorado, et al., (2018) who found that in people with a SCI, present moment awareness and being nonjudgemental about thoughts and feelings, two aspects of mindfulness associated with acceptance, magnifies the effects of pain catastrophizing on pain outcomes.

Where SCI is concerned therefore, the results of this study support Henwood, Ellis, Logan, Dubouloz and D'Eon (2012) who suggest that seeking pain resolution is a necessary stage to go through before an individual with SCI is able to live an active life in the presence of pain. In this way, mindful awareness may not provide a useful route to acceptance, whereas trying to solve the problem of pain might. Therefore, the notion of pain acceptance needs to be considered in the light of the SCI and it should not be assumed that this concept works in the same way as it does in the able-bodied pain population. It represents one way in which people with pain and SCI differ from people with pain in other populations, therefore providing an explanation for the differences found in the efficacy of some pain management programmes.

11.1.2 Comparison of in-patients T1 and T3 and out-patients in appraisal of injury

It might be expected that over time people would adjust to their disability and its consequences, appraising it more positively than in the immediate weeks

and months following injury. However, this was not the case as out-patients showed significantly lower resilience and significantly higher catastrophic negativity than in-patients at T1 in their appraisal of their SCI. As with pain acceptance, this could be associated with the high level of professional support available to in-patients (Craig, Guest, Tran, Nicholson Perry & Middleton, 2017; New et al., 2012), whereas out-patients have a range of challenges with which they need to cope without healthcare professionals on hand to assist (Craig et al., 2017; van Loo, Post, Bloemen, & van Asbeck, 2010).

Appraisal is said to consist of three dimensions: threat, loss, and challenge (Ferguson, Matthews & Cox, 1999). Once patients leave hospital the appraisal of threat associated with their injury in respect of the day-to-day difficulties of activities of daily living, and with the risk of further physical complications such as urinary tract infections and pressure sores, is likely to increase substantially. In support of this, various research has found that negative appraisals of injury predict increased distress and greater anxiety some years after discharge from hospital (Eaton, Jones & Duff, 2018; Kennedy, Kilvert & Hasson, 2016; Kennedy, Lude, Elfström & Smithson, 2010), suggesting that the injury continues to be perceived as threatening beyond rehabilitation, as indicated by this study.

Although individuals in this study demonstrated lower resilience once back in the community, having resilience makes it more likely that people will perceive their injury as less threatening, and frame it more as a challenge (Bonanno, Kennedy, Galatzer-Levy, Lude, & Elfström, 2012). They are also more likely to be accepting of their pain (Ramírez-Maestre, Esteve, & López-Martínez, 2014), demonstrating an association between appraisal of injury and pain acceptance. This could explain why in this study pain acceptance and resilience were both found to be lower in the out-patient group than in the in-patient group. The fact that people displayed less resilience following discharge from hospital supports the idea that the perceived threat associated with SCI increases. Qualitative studies have also described how patients in a community setting view the pain they experience as a threat, relentlessly

attacking them (Hearn et al., 2015). This may serve to intensify the more generally perceived sense of threat that people already experience about their injury. Therefore, the results of this study suggest that the combination of a SCI and pain may be particularly likely to generate a feeling of endangerment, resulting in catastrophic negativity, reduced resilience and lower pain acceptance.

Similarly, the appraisal of loss is likely to rise as individuals are faced with the realities of what they can no longer do (Martz, Livneh, Priebe, Wuermser & Ottomanelli, 2005). In a qualitative study, Dickson, Allan, and O'carroll (2008) report that people with a SCI experience a perceived loss of independence, loss of control and loss of identity. This has also been found in people who have lived with their SCI for some time, with perceived loss of physical resources being associated with psychological well-being (de Roon-Cassini, de St. Aubin, Valvano, Hastings & Horn, 2009). These studies suggest that the perception of loss is widespread, and associated with many aspects of the individual's life. This combination of an increased perception of threat and loss is likely to result in the reduced resilience and increased catastrophic negativity in appraisal of injury found in this study. This supports the idea that appraisals can influence coping, and coping then goes on to influence appraisals (Dean & Kennedy 2009), and that as time passes, new appraisals are made based on additional information received (Duff & Kennedy, 2003).

As with acceptance, after a nine-month period at the third time point, the differences between the in-patient and out-patient groups in the way they appraised their disability were no longer present. This once again supports the notion that appraisals continue to occur beyond the acute stages of injury and that once people leave hospital the challenges they face can undo some of the gains made during rehabilitation (Craig et al., 2017; Quartana, Campbell & Edwards, 2009).

11.1.3 Comparison of significant other responses

Where partner responses were concerned, there was no significant difference

between the degree of distracting or negative responses received by in-patients at either time point and out-patients from a significant other person. This implies that significant others' responses remain as negative or distracting once people are back in the community as when they first had their injury. However, at the first time point in-patients received significantly more solicitous responses than out-patients, but this difference had disappeared by time three. This could be explained by caregiver burnout or by cognitive bias. Where caregiver burnout is concerned, someone who has recently experienced their SCI requires a great deal of support (Post, Bloemen & de Witte, 2005). The higher number of solicitous responses received by in-patients might reflect family member's or friend's natural reactions to the early days of their injury. As the challenges associated with the injury and the pain persists through transition to the community, family and friends might find their ability to care is depleted, resulting in reduced solicitousness.

This supports research finding that over time, pain catastrophizing leads to a reduction in social support more generally (Newton-John, 2013; Cano et al., 2012). In the able-bodied population carer burnout has been related to equity theory (Adams, 1965), which states that people will experience distress if they do not perceive that what they put into a relationship is equal to what they get out of it. Carers of individuals with SCI may perceive that over time, they are putting in a great deal more than the injured person and that their own needs are not being met. This can result in a diminishing of the emotional resources needed for caring, which can in turn lead to guilt about not doing enough, resulting in further emotional exhaustion (Ybema, Kuijer, Hagedoorn, & Buunk, 2002). This has been found amongst carers of stroke survivors, where the burden of caregiving is substantially increased if the relationship is not perceived as equitable (McPherson, Wilson, Chyurlia, & LsClerc, 2011), supporting the idea that carers need to receive something back from those they are caring for. This could be in the form of emotional support and demonstrations of care and concern (Newton John, 2013).

Another possible explanation for the fewer solicitous responses received by out-patients in comparison to in-patients concerns negative cognitive biases.

The results have suggested that once people leave the supported environment of hospital, resilience and acceptance reduce and catastrophic appraisals of injury increase. This level of distress could lead to individuals only noticing the negative responses and not detecting the solicitous ones, as has been suggested by Newton John (2013). However, this study did not find that out-patient participants reported more negative responses than in-patients, which would be expected in this were the case. Therefore, it is possible that the negative bias could take the form of the individual perceiving what is meant as a solicitous response more negatively because it might not be sufficient in meeting their needs, even if the response is adequate. This may particularly be the case where pain is exacerbating the level of distress. This would support Boothby, Thorn, Overduin, and Ward (2004) who found that people classed as high catastrophizers tended to rate partner responses as less solicitous and more punishing. Therefore, the higher distress caused by the combination of a SCI and pain might make people less likely to recognise solicitous responses when they are offered, even if they do not class them as negative. It is also important to consider that solicitous, negative and distracting responses are not necessarily independent of each other, and that one type of response may be perceived in relation to another. Further qualitative research with individuals with SCI and their partners could shed further light on how partner responses are intended and received, and whether cognitive bias or caregiver burnout explains the difference in solicitous responses between in-patient and out-patient participants. This in turn could inform dyadic partner-patient interventions, which could be included in pain management programmes.

The reduction in solicitous responses in the out-patient group could help to explain why pain acceptance and resilience were higher in the in-patient T1 group and catastrophic negativity was higher in the out-patient group. Widerström-Noga, Felix, Cruz-Almeida, and Turk, (2007) found that despite having high levels of pain, people with SCI who received more solicitous and distracting responses from others had lower levels of distress, less pain interference and higher activity engagement. It is possible that this type of social support is an important factor in achieving pain acceptance and

maintaining activity levels for people with SCI. This in turn could improve the way the injury is appraised. Resilience and pain acceptance have been closely associated (Ramírez-Maestre, Esteve, & López-Martínez, 2014) and therefore solicitousness from friends and family might also enable people with SCI to sustain their resilience.

The idea of solicitousness being beneficial in the spinal cord injured population supports Stroud, Turner, Jensen, and Cardenas, (2006) who, in contrast to the able bodied population, found no relationship between solicitous responses and activity interference. Rather, it has been reported that the type of support that enables an individual with SCI to engage in valued activities and activities of daily living is essential in the process of adaptation to injury (Duggan, Wilson, DiPonio, Trumpower, & Meade, 2016). Solicitousness could be the type of response that achieves this for people with SCI. It is possible, therefore that solicitousness has greater value when people require more hands on help in order to maintain an active life. The reduction in solicitous responses in the out-patient group, therefore, might have contributed to their lower pain acceptance, reduced resilience and more negative injury appraisals.

11.1.4 Comparison between in-patient T3 and out-patient groups

The only difference between in-patients at time three and out-patients was in mood, with in-patients showing significantly higher levels of depression than out-patients. Given the previous results, it might have been expected that mood would be lower in the out-patient group, as they showed less pain acceptance and a more negative appraisal of their injury. However, as the majority of the in-patient group had recently been discharged from hospital at the third time point, it is possible that the higher depression scores are indicative of very recently having to cope without the significant support of health professionals in the safe environment of a hospital such as Stoke Mandeville. This supports Craig, Tran and Middleton, (2009), who found a lower rate of depression amongst people with SCI living in the community than for those during rehabilitation but is in contrast with Craig et al. (2015) where

depression levels maintained up to one-year post injury. However, in this last study people one-year after their injury had fairly recently been discharged from hospital (six months on average), which would reflect the findings of this research. Earlier studies have also found that depression scores peak when people first leave hospital, reducing as they adjust back into the community (Richards, 1986; Bonanno et al., 2012), although Ullrich et al. (2013) only found this to be the case when depression presented alone. When depression was comorbid with pain, scores remained high over a three year period suggesting that comorbidity caused an amplifying effect, which is not consistent with this study. The only obvious difference between the data sets is that Ullrich et al. used a sample of veterans whereas in this study participants had various causes of SCI, although it is not clear why this should make a difference.

Bonanno et al. (2012) reported finding two patterns of symptoms where depression is concerned: elevated symptoms at the acute stage which reduce over time, suggestive of recovery and adaptation, and lower symptoms early on which gradually increase with time. However, in their study Bonanno et al. found that the biggest increase in depressive symptoms occurred during the first year following injury, with only slight increases occurring in the second year. Given that out-patients in this study were all more than two years post injury, this might reflect on-going improvement in mood, explaining the difference between in-patients and out-patients. It suggests that even if other difficulties maintain over time, mood might improve, reflecting at least some adjustment to the circumstances, and a developing confidence in their ability to cope.

Overall, the results of the comparison between in-patient and out-patient participants provide partial support for the hypothesis that differences would be found on all measures. Out-patients exhibited lower pain acceptance, lower resilience, greater catastrophic negativity and fewer solicitous responses from a significant other than in-patients at time one, and lower depression than in-patients at time three. This adds weight to the idea that in many respects people with a SCI continue to struggle after they have left hospital and that a

greater degree of on-going support for out-patients would be beneficial.

11.2 Predictions of pain intensity, life interference and pain-related distress

11.2.1 Negative psychological predictors of pain-related outcomes

Hypothesis two predicted that the negative psychological variables perceived stress, pain catastrophizing, mental defeat, depression and anxiety would predict increased pain intensity scores on the combined in-patient and out-patient data sets, and an increase in the extent of life interference from pain and levels of pain-related distress on the out-patient data set. This combination of factors weakly predicted pain intensity, explaining 16% of the variance. Perceived stress and pain catastrophizing each contributed significantly, with higher pain catastrophizing predicting greater pain intensity and higher perceived stress predicting lower pain intensity.

It might have been expected that raised stress levels would be associated with increased pain as the underlying physiological mechanisms for both are similar and it is unclear why this was not the case. It is possible that psychological pain or distress caused by higher stress levels has greater negative valency than physical pain, so that greater attention is paid to it rather than to the physical pain being experienced (Eccleston & Crombez, 1999). This could then result in lower pain being reported. This would support the cognitive-affective model of pain which proposes that because emotions are as demanding of attention as pain, and individuals only possess finite attentional resources, less attention is available for the pain (Eccleston and Crombez, 1999). Neuroimaging studies suggest that attention has a modulating effect on descending inhibitory pain mechanisms so that when attention is drawn away from pain, the perception of pain is inhibited (Wiech, Ploner & Tracey, 2008; Wiech et al., 2005). Additionally, experimental studies have shown that mental stress and an increase in stress reactivity is associated with reduced pain perception (Terkelsen, Andersen, Mølgaard,

Hansen & Jensen, 2004; Diener et al., 2012). Therefore, psychological stress that grabs attention may result in a reduction in pain intensity ratings through inhibitory processes. Further research is needed to clarify the nature of the relationship between pain and perceived stress in order to fully understand the results of this study. In general, the combination of perceived stress, pain catastrophizing, mental defeat, depression and anxiety only explained a small amount of the variance in predicted pain intensity suggesting that other variables are involved in the degree of pain experienced by people with a SCI.

Where pain catastrophizing is concerned the results obtained here also contradict recent research which has generally found no association between catastrophic thinking and pain intensity (Finnerup et al., 2016) but a stronger relationship between catastrophizing and other pain-related outcomes, such as pain interference (Kim, Williams, Hassett, & Kratz, 2019). It might, therefore, have been expected that catastrophic thinking would have been influential in predicting life interference and distress but this was not the case, its only influence being related to an increase in pain intensity. Earlier research has suggested that catastrophic thinking predicts both the reported intensity of pain and the degree of pain interference (Molton et al., 2009; Nicholson Perry, Nicholas, & Middleton, 2009), but this has not consistently been found in more recent years.

The differences found between studies might partially be explained by the fact that this model included pain catastrophizing as a single construct, rather than including the three different elements of catastrophic thinking (rumination, magnification and helplessness) individually. When these different elements were placed in a regression model, along with perceived stress, the model significantly predicted pain intensity, life interference and pain-related distress. Lower stress and increased helplessness were the only significant contributors in predicting higher pain intensity, explaining more of the variance (22%) than when pain catastrophizing as a whole was included. This supports Craner, Gilliam and Sperry, (2016), who also identified helplessness as a predictor of pain severity, and Vienneau, Clark, Lynch, and Sullivan (1999) who found that helplessness predicted both pain intensity and pain-related distress. The

results concerning in-patient and out-patient differences, discussed above, found that out-patients were less resilient and more prone to catastrophic negativity. It is possible that a sense of helplessness, as measured by the PCS (Sullivan, Bishop & Pivik, 1995), increases as resilience lessens and appraisal of injury worsens. Feeling helpless with regards to pain, might increase the fear or worry associated with it, ensuring it remains the focus of attention and thus increasing its perceived severity, supporting both the Misdirected Problem Solving (Eccleston & Crombez, 2007) and Fear-Avoidance (Vlaeyen & Linton, 2000) models of pain.

This regression model, with the sub scales of pain catastrophizing and perceived stress, also significantly predicted greater life interference. A tendency to magnify the impact of pain was the only variable contributing to this, explaining an average of 43.5% of variance. Pain magnification did not contribute to the prediction of either of the other two pain outcomes which is in contrast to earlier studies which found it to be significantly associated with pain severity (Sullivan, Stanish, Sullivan & Tripp, 2002; Lefebvre, Lester & Keefe, 1995). More recently research has found magnification to be a better predictor of anxiety and depression (Adachi et al., 2019; Iwaki et al., 2012; Craner et al., 2016), physical quality of life (Iwaki et al., 2012; Craner et al., 2016) and, as with this study, pain interference (Craner et al., 2016). This suggests that the effects of magnification do not impact directly on the sensory aspects of pain as helplessness does, but have a greater influence on the affective dimensions and resulting life interference. This supports Sullivan et al. (2005) who found that pain catastrophizing as a whole is more closely associated with the affective pain experience. It is possible that the prolonged recovery from SCI and the ongoing challenges associated with it result in increased magnification as the seriousness of the injury remains apparent. In turn, magnification might keep attention focused on pain (Sullivan et al., 2002). In this way, magnifying the impact of pain might indirectly lead to activity avoidance as people remain fearful of the pain they are experiencing, explaining why magnification predicts greater life interference.

Where the third dimension of pain catastrophizing is concerned, this study, did

not find that rumination contributed to the prediction of any pain-related outcomes, which concurs with Craner et al. (2016), who found that rumination was not a unique predictor of pain. It is not clear why rumination did not predict pain outcomes, and Craner et al. were also unable to offer an explanation. Other studies have found that rumination predicts pain-related disability, which is a form of life interference, (Sullivan, Stanish, Waite & Sullivan, 1998) and pain interference more generally (Adachi et al., 2019). Greater rumination has also been associated with increased pain and distress (Gilliam et al., 2010; Van Damme, Crombez, Bijttebier, Goubert, & Van Houdenhove, 2002). However, research has generally found magnification and helplessness to be more influential on pain outcomes than rumination (Craner et al., 2016; Iwaki et al., 2012), which is supported by this study.

Surprisingly, none of the catastrophizing sub scales contributed to the prediction of pain-related distress, with perceived stress being the sole contributing factor in this model, explaining 60% of variance. This is unexpected because catastrophic thinking has itself been described as a means to communicate the distress being experienced (Sullivan, 2012; Junghaenal, Schneider and Broderick, 2017). It is also at odds with research associating catastrophic thinking and distress in the spinal cord injured population (Nicholson Perry, Nicholas & Middleton, 2009). Even with mobility controlled for, pain catastrophizing has been associated with lower positive affect and higher depression (Kim, Williams, Hassett, & Kratz, 2019) and for people with neuropathic pain, high catastrophizing is associated with increased psychological distress (Gruener, Zeilig, Laufer, Blumen & Defrin, 2017). It is unclear why the results of this study are incompatible with previous research. It is possible that people with SCI and higher distress experience greater disability because of it, so that distress is conceived as being interference from pain, which would explain this result. However, further research is needed to confirm this. Overall, these results support the notion that whilst each of the catastrophizing subscales together form pain-related catastrophic thinking generally, they are each quite distinct factors that impact on different pain outcomes in different ways.

The model of perceived stress, pain catastrophizing, mental defeat, depression and anxiety more strongly predicted the degree of distress individuals experienced because of their pain and the degree to which pain interfered with their normal activities than it did pain severity, explaining an average of 72% and 56% of variance respectively. However, the contributing factors were limited to depression and perceived stress. Perceived stress only contributed to predicting an increase in distress. This latter result supports the earlier suggestion that higher psychological distress might divert attention from pain, explaining the reduced pain intensity predicted by higher perceived stress. It is unsurprising that higher perceived stress predicts greater pain related distress given that both are associated with HPA (HPA) axis activity. Carlesso, Sturgeon and Zautra, (2016) suggest that the increased threat associated with pain causes a dysregulation of cortisol production. It is likely that when an individual feels highly stressed, they will perceive the threat of pain to be greater, resulting in greater distress. This is supported by research finding that both perceived psychological stress (Lebares et al., 2018) and physiological markers of stress in the form of diurnal cortisol patterns (Staufenbiel et al., 2012), are associated with depression and anxiety, which represent a form of psychological distress (Lebares et al., 2018).

Higher scores on the depression sub scale of the HADS were particularly influential in predicting an increase in both pain-related distress and life interference from pain, although they did not predict increased pain intensity. Where the first two pain outcomes are concerned, this is consistent with the large body of evidence from previous studies (e.g. Tran et al., 2016; Craig et al., 2017). On its own depression can result in psychological distress and low motivation, and this can be amplified when coupled with pain and disability (Xiaoyu, 2018). However, it is in contrast with studies in SCI which have found an association between depression and increased pain (Battalio, Glette, Alschuler, & Jensen, 2018; Craig, Guest, Tran, Nicholson Perry & Middleton, 2017; Ullrich et al., 2013). It might be that the effect of depression on pain intensity is mediated by other factors not identified in this regression analysis, suggesting that, if this were the case, depression only affects pain intensity indirectly through a mediating variable and does not have a direct effect on the

severity of pain. The mediation analysis in this study supports this notion. Depression did have an indirect effect on pain intensity when mediated by pain catastrophizing, but it did not affect pain directly.

The mediated association between depression and pain intensity supports the Örebro Behavioural Emotion Regulation Model (Linton and Bergbom, 2011). This model suggests that a pain or depression flare-up results in catastrophic thinking and negative emotions. If this is not regulated, it can lead to a relapse of low mood and pain-related disability causing further catastrophizing. As this cycle is repeated, with continued emotion regulation failure, the relationship between depression and pain becomes firmly established, and more likely to trigger catastrophic worry. This then results in the perpetuation of the vicious cycle and on-going pain (Linton and Bergbom, 2011). The model was proposed to explain pain and depression in the able-bodied pain population. However, the results of this study support the important role of pain catastrophizing where depression and pain are concerned and suggest that without catastrophizing, the impact of low mood on pain intensity would be far less. As suggested by Linton and Bergbom (2011), it is catastrophic thinking that mediates this relationship and this is also the case for people with a SCI. The implication of this is that a focus on mood when considering pain management will not be sufficient to reduce the negative outcomes of pain. Catastrophic thinking will need to be targeted to halt the vicious cycle described by Linton and Bergbom (2011). A full discussion of the results of the mediation analyses can be found below in Section 11.5.

It is of note that in this regression model neither mental defeat or anxiety contributed significantly to the prediction of any of the pain outcomes. This is in contrast with much of the literature. Mental defeat has widely been associated with various aspects of pain, such as affective pain (Hezeldene-Baker, Salkovskis, Osborn, & Gauntlett-Gilbert, 2018), pain severity (Tang, Shum, Leung, Chen and Salkovskis, 2013), pain interference (Tang et al., 2013), and suicidal ideation which is indicative of psychological distress (DeCaria & Patel, 2018; Tang, Beckwith & Ashworth, 2016). Similarly, anxiety is associated with and been found to predict pain intensity (Csupak, Sommer,

Jacobsohn, & El-Gabalawy, 2018) and is associated with life interference and pain-related disability (Battalio et al., 2018). Why this study had such contrasting results is unclear. However, as with depression and pain intensity, it suggests that rather than directly affecting pain-related outcomes, as implied by previous research, mental defeat and anxiety have an indirect effect mediated by some other variable. This is borne out by the mediation analysis of this study where anxiety and mental defeat indirectly affected various pain outcomes when mediated by pain catastrophizing and/or appraisal of injury. The results of the mediation analyses is discussed in Section 11.5 below.

In line with most of the other negative psychological characteristics, catastrophic negativity as a way of appraising the injury did not contribute significantly to the prediction of pain intensity ratings. However, it was much more influential with regards to the other pain-related outcomes. Greater catastrophic negativity predicted increased life interference from pain and higher levels of pain-related distress, explaining 47% and 31.5% of the variance respectively. These results reflect earlier studies that have associated negative appraisals of injury with poorer perceived quality of life (van Leeuwen, Kraaijeveld, Lindeman, & Post, 2012), greater psychological distress (Kennedy, Kilvert & Hasson, 2016), and reduced functional ability in terms of daily living activities (Kennedy et al., 2010). However, this study builds on this by identifying negative injury appraisal as a contributing factor to the distress and life interference experienced by people with SCI and pain. As stated earlier, it is likely that people appraise their injury as threatening and associate significant losses with it (Martz, Livneh, Priebe, Wuermser & Ottomanelli, 2005). When pain is also present the sense of threat and loss will be magnified (Hearn et al., 2015), resulting in increased distress. The heightened fear associated with threat and loss might result in people reducing their activities as a way of protecting themselves from further psychological and physical stress. In this way a negative appraisal of injury, together with a magnified sense of threat and loss due to pain, may result in the greater life interference and distress suggested by this study. Given that catastrophic negativity was higher amongst the out-patient participants than the in-patients (see above), and that it is a significant predictor of on-going distress and

disability related to pain, these results suggest that appraisal of injury is a key factor to consider in pain management during rehabilitation but also that this focus needs to be continued following transition to the community.

In summary, the combination of perceived stress, pain catastrophizing, mental defeat, depression and anxiety predicted pain intensity ratings, (pain catastrophizing contributed to increased pain intensity and perceived stress predicted lower pain intensity), life interference, (higher depression contributed to higher interference), and pain-related distress, (both higher depression and higher perceived stress predicted greater distress). When the subscales of pain catastrophizing were entered into a regression model with perceived stress, lower stress and higher helplessness predicted increased pain intensity, pain magnification predicted increased life interference, and higher stress predicted greater distress. In a linear regression model, higher catastrophic negativity as an appraisal of disability predicted greater life interference and pain-related distress. This partially supports the second hypothesis that negative psychological variables would predict increases in pain intensity, life interference and pain-related distress.

11.2.2 Positive psychological predictors of pain-related outcomes

The third hypothesis predicted that the positive psychological characteristics of determined resilience (with regards to appraisal of injury), combined with the two subscales of the CPAQ (activity engagement, and willingness to live life in the presence of pain (pain willingness); McCracken, et al., 2004) would predict lower pain intensity scores on the combined in-patient and out-patient data sets, and reduced life interference from pain and lower levels of pain-related distress on the out-patient data set. This hypothesis was partially supported. The model did not predict ratings of pain intensity, however, when combined with pain willingness and engagement in activities, pain interfered less in people's lives when they appraised their disability less negatively, demonstrating higher resilience. The model only explained a relatively small amount of the variance (an average of 16%) and resilience was the only

contributing factor, but it suggests that the way disability is appraised can have a significant effect on some of the consequences of pain, even if it does not affect pain intensity itself.

This supports earlier research suggesting that the challenges associated with rehabilitation and adjustment to injury are met more successfully when resilience is high (Bonanno, Kennedy, Galatzer-Levy, Lude, & Elfström, 2012). This is important where SCI is concerned because of the importance of functional adaptation, that can be significantly disrupted by pain (Gruener, Zeilig, Laufer, Blumen & Defrin, 2018). Additionally, resilience has been identified as a key facilitator in adjustment to injury, but pain can be a barrier to developing resilience (Duggan, Wilson, DiPonio, Trumpower & Meade, 2016). This highlights the importance of resilience in both pain and SCI and it implies that for pain management to be effective, interventions that boost resilience should be included during rehabilitation. This is particularly the case given the notion that resilience may not be a stable trait, but a characteristic that can be developed (American Psychological Association, 2019), with the potential for improving outcomes for people with SCI. Additionally, as pain acceptance did not contribute to life interference from pain, as it has been suggested it does in previous research (e.g. Craner et al, 2017), the results from this study imply that in SCI, resilience is a much more significant factor where coping with the combination of the injury and pain is concerned. As previously discussed, it is possible that pain acceptance is achieved in different ways in SCI, and that it represents less of a contributing factor to adaptation.

The combination of resilience, pain acceptance and activity engagement also predicted pain-related distress, with resilience and activity engagement being particularly influential and explaining an average of 33% of variance. When people demonstrated greater resilience, distress was lower, supporting Ong, Zautra and Reid, (2010) who associated resilience with more positive emotions and less catastrophic thinking. However, when activity engagement was higher, pain-related distress increased, suggesting the more active or engaged in activities people are, the more distress it causes them.

This provides further evidence that pain acceptance may be different in the spinal cord injured population, and that it may not always represent a positive outcome for people. Previous research has found mixed results with regards to pain acceptance with some studies suggesting that pain catastrophizing exerts greater influence on all pain outcomes than pain acceptance (Elvery, Jensen, Ehde, & Day, 2017), and others finding that catastrophic thinking is more closely associated with psychological distress and acceptance is more closely associated with physical functioning (Gillanders, Ferreira, Bose, & Esrich, 2012; Esteve, Ramírez-Maestre, & López, 2007). This is at odds with the results of this study where resilience, rather than pain acceptance was associated with life interference, and acceptance in the form of activity engagement predicted greater distress.

It is possible that for people with SCI, increased activity engagement has many more challenges associated with it than in the able-bodied population, and that these challenges lead to greater distress. It is also possible that although activity engagement causes increased pain and discomfort, this may not necessarily be a negative outcome. It could be part of living life in the presence of pain, which ultimately brings increased functional independence and greater life satisfaction despite an increase in pain-related distress. This could be a plausible explanation given that higher pain acceptance has been found to result in increased activity engagement (Kratz, Ehde, Bombardier, Kalpakjian & Hanks, 2017) and better quality of life (Kim, Williams, Hassett, & Kratz, 2019). An improvement in functioning therefore, may not be dependant on improved emotion regulation or reduced pain (Akerblom, Perrin, Fischer & McCracken, 2016).

The results from this study support the notion that activity engagement and pain willingness impact differently on pain outcomes. Pain willingness did not contribute to the prediction of any of the pain outcomes measured, whereas activity engagement contributed to predicting increased distress. Earlier studies, too, found that activity engagement had a stronger impact on various pain outcomes in the able bodied population, with pain willingness not having a significant influence (Fish, McGuire, Hogan, Morrison & Stewart, 2010).

Kratz, Hirsh, Ehde and Jensen, (2013) suggest this might be because pain willingness is more likely to impact on the more negative indicators of adjustment such as depression, whereas activity engagement can be influential in both. This study did not assess depression as an outcome of pain, but as a predictor. Given there have been relatively few studies analysing pain acceptance in SCI, and that the results are mixed with regards to its influence, it is important for future studies to explore further the way in which acceptance of pain might impact on pain-related outcomes and subsequent adjustment to disability.

In summary, the third hypothesis was partially supported. The regression model of resilience, activity engagement and pain willingness did not predict pain intensity ratings, but did predict life interference (with increased resilience predicting greater interference), and pain-related distress (greater resilience predicted lower distress and greater activity engagement predicted higher distress). Overall, these more positive responses to pain and to SCI tended to predict life interference and distress more weakly, explaining less of the variance, than the negative responses, therefore, it appears that negative psychological variables might have a stronger impact. It may be more important to focus on reducing the negative factors rather than focusing on increasing the positive factors when pain management is considered.

11.2.3 How the response of a significant other predicts pain-related outcomes

Intrapersonal characteristics were not alone in predicting the consequences of pain. Hypothesis four predicted that the way in which a significant other person responded to the individual in pain would predict pain intensity, pain interference and pain-related distress. The responses measured were distracting responses, solicitous responses and negative responses and the hypothesis was partially supported. None of the response categories predicted pain intensity, however, a significant other response did predict life interference, explaining an average of 33% of the variance. When a significant other person responded in a negative or distracting way to an individual in

pain, it contributed to an increase in life interference. This is unsurprising where a negative response is concerned and supports previous literature in the able-bodied pain population which has associated negative responses from a significant other with worsening pain behaviour (Burns et al., 2018) and poorer wellbeing (Song, Graham-Engeland, Mogle & Martire, 2015).

However, where a distracting response is concerned this is in contrast with Widerström-Noga, Felix, Cruz-Almeida, and Turk, (2007) who found a reduction in life interference was associated with receiving distracting responses. It also conflicts with evidence suggesting that the kind of support that people with SCI most value, is that which encourages resilience and adaptation, rather than removing responsibilities from the individual (Duggan et al., 2016). A distracting response might be thought of as encouraging adaptation and is generally considered to be a positive way of responding (Henwood & Ellis, 2004), taking the individual's attention away from their pain, and it was not expected that this would increase life interference. It might be that for people with SCI a distracting response is seen simply as someone interfering, or challenging them to greater activity engagement, which may or may not be a positive thing. This is consistent with the results discussed above, which found that increased activity engagement predicted greater pain-related distress. Therefore, where SCI is concerned, distracting someone in pain by encouraging engagement in tasks or hobbies might represent unnecessary and unwelcome interference, resulting in increased distress.

Alternatively, a distracting response might be seen as being dismissive of the individual's pain, and not taking seriously the challenges associated with pain and SCI. However, Widerström-Noga et al., (2007) and Duggan et al., (2016) both carried out their research on spinal cord injured participants, and it is not clear what may have influenced the conflicting result in this study. There is evidence of distracting responses having a negative impact more generally in the spinal cord injured population, for example, they have been associated with higher pain (Taylor et al., 2012) and higher depressive symptoms (Stroud, Turner, Jensen, & Cardenas, 2006). With studies finding such variation in their results further qualitative research is needed to determine how individuals

perceive these categories of responses, and what, for example a distracting response might mean to people with SCI and how it might be interpreted.

The model of distracting, solicitous and negative responses also significantly predicted pain-related distress, explaining an average of 19% of variance. As might be expected, negative responses from another person contributed to the prediction of higher distress, but a distracting response was not a contributing factor. Negative responses from a significant other have consistently been associated with poorer pain outcomes, including increased pain, higher depressive symptoms, relationship distress and are generally thought to be detrimental to the individual's well-being (Burns et al., 2018; Pow, Stephenson, Hagedoorn, & Delongis, 2018; Song, Graham-Engeland, Mogle, & Martire, 2015). The results of this study support this, adding to the body of research indicating that negative or punishing responses increase the distress that individuals feel as a result of their pain.

An unexpected result was that solicitousness did not contribute to the prediction of pain intensity, distress or life interference from pain. Most previous research has found a negative effect of solicitous responding both in the able-bodied population (Hemphill, Martire, Polenick, & Parris Stephens, 2016; Kostova, Caiatta-Zufferey, & Schulz, 2014) and amongst people with SCI (Fogelberg, Hughes, Vitiello, Hoffman, & Amtmann, 2016; Vriezekolk, Peters, van den Ende, & Geenen, 2019), so it might have been expected that this would be reflected in this study. This was not the case, with distracting and negative responses having a much greater influence. As discussed earlier, it is possible that solicitousness in the spinal cord injured population does not result in the negative outcomes seen in the able-bodied population. Rather, a solicitous response may have benefits for people with SCI in that it may enable them to engage in activities necessary for adjustment and help them to work towards greater independence. The suggestion that solicitousness might be helpful in this group of people however, requires further research as it did not predict either an increase or reduction of pain outcomes in this study.

In summary, solicitous, negative and distracting responses from a significant other to someone in pain predict the degree of life interference from pain and the level of pain-related distress. A greater number of negative and distracting responses contributed to an increase in life interference, whereas only negative responses contributed to greater pain-related distress. Solicitousness did not contribute to the prediction of any of the pain outcomes. That social responses predicted certain pain outcomes supports the literature implicating social support more broadly in the consequences of pain (Sullivan, 2012; Craig, 2009) and indicates that interpersonal factors are influential in the pain experience.

11.3 **The influence of cortisol**

The impact of the biological marker of stress, cortisol concentration, was analysed but did not predict pain intensity, life interference or pain-related distress. This is in contrast to the fifth hypothesis, which predicted that cortisol concentration would predict increases in each of these pain-related outcomes. Given that higher cortisol production has been consistently and closely associated with both pain and stress (or distress) conditions (Staufenbiel, Penninx, Spijker, Elzinga & van Rossum, 2012), it was expected that this would be reflected in this study. Additionally, high stress, of which high cortisol production is an indicator, has been linked to life interference from pain, even when pain intensity was controlled for (White, Jiang, Hall, Katz, & Zimmerman, 2015), but again, such an association was not found in this study. Past research has associated both hypercortisolism (Coloca & Benedetti, 2007) and hypocortisolism (Fries, Hesse, Hellhammer & Hellhammer, 2005) with pain, with the former being linked to acute stress and pain conditions and the latter to chronic stress and pain conditions. However, this research found that neither magnified nor depleted cortisol levels predicted pain outcomes.

Although it is thought that the HPA (HPA) axis might be involved in pain modulation it is unclear precisely how cortisol might contribute to this (Zouikr & Karshikoff, 2017). It has been suggested that cortisol on its own may not be sufficient to contribute to pain conditions, but that when combined with

psychological factors its influence is greater (Melzack, 2005), providing a possible explanation for these results. Therefore, given the non-significant results, it seems likely that the relationship between cortisol and these pain outcome variables may be mediated by some other factor(s), (see Decision Tree for Establishing and Understanding Types of Mediation and Nonmediation, (Zhao, Lynch & Chen, 2010) in Results - Stage 2 Analysis above), as suggested in previous research (Sudhaus et al., 2012; Doane et al., 2013).

The sixth hypothesis predicted that cortisol would be associated with each of the psychosocial variables and this was the case where pain catastrophizing was concerned, partially supporting the hypothesis. Cortisol concentration was positively related to catastrophic thinking, specifically to helplessness and rumination. It was considered therefore, that pain catastrophizing might be a key factor that mediates the relationship between cortisol concentration and pain outcomes. When this theoretical model was analysed, with pain catastrophizing being considered as a mediator between cortisol and various consequences of pain, an association was established. Cortisol concentration, mediated by catastrophic thinking predicted a wide range of pain-related outcomes: pain intensity, life interference from pain, pain-related distress, the degree of control over ones life, and the degree to which pain reduced activity engagement. In most cases the mediated effect of higher cortisol concentration predicted increased pain outcomes, apart from one; it predicted lower life control. As cortisol did not have a direct effect on any of these outcomes, it suggests that pain catastrophizing is likely to be the only mediator, supporting this hypothesised framework.

Whilst the mediating role of pain catastrophizing in the relationship between cortisol and pain has not always been found (Carlesso, Sturgeon, & Zautra, 2016), the results of this study support the larger body of research. Many studies have suggested that cortisol and catastrophic thinking are closely related, linking pain catastrophizing with an elevated diurnal cortisol pattern (Quartana et al., 2010), and with a heightened CAR (Walton, MacDermid, Russell, Koren & Va Uum, 2013). Additionally, hypercortisolism, reflected in

increased cortisol production, has been associated with increased pain sensitivity through the reduction of pro-inflammatory cytokines (Raison & Miller, 2011) further implicating cortisol as a key contributor to pain. These results suggest the route through which cortisol concentration, mediated by catastrophic thinking, impacts on pain outcomes.

As was found in this study, cortisol concentration has been associated more specifically with helplessness (Sudhaus et al., 2012), one of the sub-scales of pain catastrophizing. In the regression analysis discussed earlier in Section 11.2.1, a stronger sense of helplessness predicted greater pain intensity, a mediated outcome of higher cortisol concentration. This adds weight to the notion that the three elements of catastrophic thinking may interact with biopsychosocial variables in different ways to impact on pain-related outcomes. Overall, the results suggests that high cortisol concentration has a negative impact on a range of pain outcome measures when mediated by catastrophic thinking, supporting the idea that cortisol in combination with psychological variables is a strong predictor of the consequences of pain (Melzack, 2005).

Whilst cortisol concentration was positively related to pain catastrophizing, it was not related to any of the other variables in the study. This provides only partial support for the sixth hypothesis, which predicted an association between cortisol and all other variables. This is particularly surprising where perceived stress is concerned, given that HPA axis activity and the resulting cortisol production is part of the stress response. This lack of an association has been found in previous studies (e.g. Dowlati et al., 2010; Stalder et al., 2010) and Staufenbiel, Penninx, Spijker, Elzinga, and Rossum (2012) suggest that it might be due to the assessment methods of perceived stress and cortisol concentration. The PSS (Cohen, Kamarck & Mermelstein, 1983) requires people to answer questions related to how they felt in the last month whereas salivary cortisol reflects cortisol concentration over the previous few days at best. This difference in time would explain the insignificant result found in this study.

The fact that cortisol was not related to any variables other than pain catastrophizing is in contrast with many other studies, particularly where anxiety and depression are concerned (e.g. Engert, Efanov, Dedovic, Dagher, & Pruessner, 2011; Vreeburg et al., 2010). One possible explanation for the difference in results between this study and previous research is that many of those other studies used the CAR (CAR) in their analysis. For example, Dedovic et al. (2010) reported a lower CAR in people with major depressive disorder and Vreeburg et al. (2010) associated an elevated CAR with acute anxiety. However, it has been suggested that the CAR is distinct from the more general cortisol diurnal rhythm and as such may not be a useful biomarker of stress or a good indicator of HPA activity (Stalder et al., 2016). Salivary cortisol was gathered between 3pm and 6pm in this study which is not comparable to the CAR. However, Burke, Davis, Otte, and Mohr, (2005) found a stronger association between depression and the cortisol diurnal pattern than between depression and the CAR. Therefore the difference between the CAR and cortisol diurnal patterns may not provide a sufficient explanation as to why cortisol was not related to depression or anxiety in this study.

Another possible explanation for the lack of a significant association between cortisol and depression is that rather than being simply correlated, the relationship between them might be that of predictor and outcome. In an additional exploratory analysis, this study found that higher cortisol concentration, mediated by pain catastrophizing, predicted higher depression. Various studies have suggested that both a high CAR and cortisol reactivity more generally predict depressive symptoms (Bos et al., 2005) and major depressive disorder (Vrshek-Schallhorn, 2013). In the latter case, this occurred independently of any stressful life events. Additionally, a vulnerability for depression has been linked to HPA axis activity (Oldehinkel & Bouma, 2011) and it has been suggested that the association between psychological difficulties and changes in cortisol production might represent an underlying neurobiological trait (Adam et al., 2014). In support of this, the CAR, which is known to have a strong genetic component (Wüst, Federenko, Hellhammer, & Kirschbaum, 2000), has been associated with hopelessness, a personality trait linked to depression (van Santen et al., 2011).

Similarly, Tafet and Nemeroff (2016) have suggested that HPA axis dysregulation might represent a trait vulnerability for depression. This could explain why cortisol concentration, mediated by catastrophic thinking, predicted depression in this study, and might be particularly relevant for people with SCI. Tafet and Nemeroff's diathesis stress model suggests that a combination of genetic vulnerability, early life stress and chronic later stress might lead to the development of a central nervous system phenotype and cognitive vulnerability. This in turn would cause up-regulation of the HPA axis and increased cortisol production, leading to the emotional vulnerability and changes in molecular structures that result in depression and anxiety.

A SCI represents a significantly stressful event, and yet not everyone develops psychological distress as a result. It is possible that people who have had a less stable childhood, and who have a genetic vulnerability will experience greater distress associated with their SCI, resulting in the increased HPA activity and higher cortisol production that predicts depression. This implicates cortisol as an important factor beyond just pain intensity, but in the broader consequences of pain, both emotionally and behaviourally. It also provides additional support for the important role of pain catastrophizing where the impact of cortisol is concerned. An assessment of premorbid conditions is important, therefore, during rehabilitation as it could inform the likelihood of psychological problems developing at some stage. However, the relationship between depression and cortisol is complex and widely acknowledged not to be fully understood (Herbert, 2013; Booij, Bouma, De Jong, Ormel, & Oldehinkel, 2013; Nicolaides, Kyratzi, Lamprokostopoulou, Chrousos, & Charmandari, 2015). This is especially the case where SCI is concerned as fewer studies have looked at the relationship when SCI is involved. Future research needs to look at the combination of these factors to shed further light on how they combine and influence pain and adaptation outcomes for people with SCI, and to verify the results found in this study.

11.3.1 Cortisol concentration over time

The longitudinal study found that salivary cortisol concentration levels did not change over the nine-month period (hypothesis 7) for the in-patient participants, which did not support the hypothesis. Additionally, there was no difference between in-patient and out-patient concentration levels (hypothesis 1), despite the fact that as time since injury increases, it would be anticipated that cortisol levels would reduce. However, when the in-patient and out-patient groups were collapsed and cortisol was correlated with time since injury, the result showed that as time increased cortisol concentration did decrease, providing support for hypothesis eight where cortisol is concerned. It is expected that cortisol levels will be high in the period following a SCI, as increased HPA axis activity is a natural response to physical trauma, and this has been consistently found in previous research (Fatima, Sharma, & Verma, 2016; Campagnolo, Bartlett, Chatterton, & Kellor, 1999). What is unclear is whether the reduction in cortisol over time found in this study represents a healthy gradual return to premorbid levels, or whether it is an indication of hypocortisolism, where cortisol production is exhausted following a period of hypercortisolism (Hannibal & Bishop, 2014).

This pattern of short-term hypercortisolism followed by longer-term hypocortisolism is not uncommon following SCI (Huang, Wang, Lee, & Lai, 1998; Kalpakjian, Farrell, Albright, Chiodo, & Young, 2009) so it would not be unexpected if this was the case here. However, it is of concern because a dysfunction of the immune system can result from both an up-regulation of HPA axis activity (hypercortisolism) and also from a blunted cortisol response (hypocortisolism; Allison & Ditor, 2015). As infection is a particular risk for people with SCI, immune system functioning is extremely important. Further research, therefore, is necessary to provide clarity on the reason for the reduced cortisol production over time found in this study. Analysing cortisol concentration in hair samples would enable premorbid cortisol levels to be identified. Each centimetre of hair represents one month, therefore three centimetres of hair can determine cortisol levels three months prior to the measurement date (Walton, MacDermid, Russell, Koren & Van Uum, 2013).

This could be compared with cortisol levels in the longer term following SCI to determine whether cortisol has returned to a healthy level or whether hypocortisolism is occurring.

In summary, pain catastrophizing has emerged as an important psychological factor where cortisol production is concerned. It is the only psychosocial factor measured in this study to have a significant association with cortisol concentration levels. Additionally, rather than having a direct effect on pain outcomes, cortisol affects pain intensity, pain-related distress, life interference from pain, the degree of control over ones life, and the degree to which pain reduces activity engagement via the mediating role of catastrophic thinking. Pain catastrophizing also mediates the relationship between cortisol and depression, with increased cortisol combined with higher catastrophic thinking predicting greater depressive symptoms. This suggests that when analysing HPA axis activity in relation to pain, studies should also incorporate measures of pain catastrophizing to ensure the results reflect the relationship between cortisol and pain accurately. Lastly, cortisol concentration levels decreased as time since injury increased. Future research needs to clarify whether this represents hypocortisolism as opposed to a healthy return to premorbid levels.

11.4 **Biopsychosocial outcomes over time**

It was hypothesised (hypothesis 7) that as people adapted to their SCI their biopsychosocial outcomes would collectively improve and stabilise. For in-patients, over the nine-month period this hypothesis was not supported. Depression and the tendency to magnify the impact of pain (a sub scale of the PCS; Sullivan, Bishop & Pivik, 1995) increased over the nine months and determined resilience with regards to appraisal of injury decreased. This indicates that for people with SCI and pain, rather than adapting to their SCI, psychological outcomes might worsen over time in general and, more specifically, on leaving hospital. Although the effect sizes were small, it is in line with the in-patient and out-patient comparison study, which found that out-patients had lower resilience and higher catastrophic negativity than in-patients, and that depression was worse for the in-patients at the third time-

point than at the first time-point.

One of the demographic factors collected from in-patients and out-patients was time since injury and so it was also possible to look at the relationship between time and the biopsychosocial outcomes in this way. It was hypothesised (hypothesis 8) that there would be a relationship between each of the biopsychosocial variables and the time since injury, and this hypothesis was partially supported. The results of this correlational analysis provide further evidence of the worsening of psychological variables over time. Mental defeat and feelings of helplessness (another sub scale of the PCS; Sullivan, Bishop & Pivik, 1995) in relation to pain were positively related to time since injury, with both increasing as time since injury increased. As with the small effect sizes of the longitudinal study, the correlations are weak to moderate. However, they are significant and they are consistent with the results of both the longitudinal analysis and the in-patient and out-patient comparison studies. This study suggests therefore, that over a nine-month period, which covers the transition from in-patient to out-patient, depression and pain magnification (pain catastrophizing) increase, resilience decreases, and that as time goes on a sense of mental defeat and helplessness develop.

These results support previous research that has found a significant number of people with SCI experience worsening depression and more catastrophic thinking on transitioning to the community (Craig, Guest, Tran, Nicholson Perry & Middleton, 2017; Bonanno et al., 2012). The possible reasons for this have already been discussed in Section 11.1 above, but the fact that helplessness and mental defeat are positively correlated with time since injury and may therefore, both increase across the transition from a hospital to a community setting implies that people feel more distressed, both in terms of catastrophic thinking and in feeling defeated by their pain. When the definitions of these two concepts are considered, it is clear that they are related constructs. Mental defeat is defined as giving up one's will and identity to the pain, and feeling defeated by it (Ehlers, Maercker and Boos, 2000) and helplessness, as an element of catastrophic thinking, is explained as feeling there is nothing that can be done about the pain, and feeling helpless in the presence of it

(Sullivan, Bishop & Pivik,1995).

Tang, Salkovskis and Hanna (2007) propose that, whilst both are forms of catastrophic thinking, there are subtle differences between mental defeat and pain catastrophizing. They posit that pain catastophizing focuses on the experience of the pain, whereas mental defeat focuses on the effects of pain and how it strips away a sense of autonomy from the individual. It is likely therefore, that an individual with SCI and in pain will have negative catastrophic thoughts about how bad the pain is and a sense of helplessness with regards to what the consequences of it may be for them given their disability (pain catastrophizing). Alongside of this they may also feel defeated by the pain and view it as an attack on their identity, which has already been challenged by the life-changing injury (mental defeat). In this way helplessness and mental defeat might combine to be particularly problematic for people with a SCI and it is unsurprising that they both increase in line with time since injury. It is likely, therefore, that mental defeat and pain catastrophizing each contribute to the other (Tang et al., 2007). Once again, this implies that pain catastrophizing, in the form of helplessness in this instance, has a key role, and combines with psychological variables, such as mental defeat, increased depression and reduced resilience, to influence the experience of pain.

Combined, these results provide compelling evidence to suggest that rather than adapting and adjusting positively to a SCI, when pain is also present, people experience a worsening of psychological factors over time. Given that there is less professional support available once people have completed their in-patient rehabilitation and are back in the community (Craig et al., 2017; van Loo, Post, Bloemen, & van Asbeck, 2010), this is of particular concern. It indicates that a much greater emphasis needs to be placed on continuing support following transition from hospital to the community and that rehabilitation services should be extended to include the out-patient community. This is particularly important if people with a SCI are to achieve a good quality of life and engage in activities that are important to their wellbeing.

11.5 Mediation analysis

In the regression analysis discussed earlier, only a few of the biopsychosocial variables contributed to the prediction of pain-related outcomes. In response to this and because the wider literature suggests that certain variables might mediate the effects of biopsychosocial factors on pain outcomes (e.g. Furrer, Michel, Terrill, Jensen, & Müller, 2019; Pinto-Gouveia, Costa, & Marôco, 2016) mediation analyses were undertaken. This second stage of the overall analysis was exploratory and sought to discover what might mediate a relationship between biopsychosocial factors and the pain outcomes of pain intensity, life interference, pain-related distress, support, life control, activity level (MPICa), and the degree to which activities had been reduced by pain (MPICb). Four mediators were analysed: pain catastrophizing, pain acceptance, catastrophic negativity and determined resilience, the latter two relating to the two types of appraisal of SCI (Dean & Kennedy, 2009). In mediation analysis, where indirect effects are discussed, this refers to the effects of the predictor on the pain outcome, via the stated mediator. Direct effects are the effects of both the predictor and mediator on the outcome as a regression model. Total effects refer to the effect of the predictor on the outcome without the mediator included in the model. If there is only an indirect effect, it suggests that the theoretical framework is accurate and no other mediator is involved. However, if there is also a direct effect it suggests that the framework tested is incomplete and it is likely that other mediator(s) may have been omitted. In this case, further research will be necessary to explore what other mediators might be involved.

11.5.1 Pain catastrophizing as a mediator

Pain catastrophizing emerged as a particularly strong mediator between many of the biopsychosocial factors and pain outcomes. This was particularly the case where cortisol concentration (as discussed earlier in Section 11.3), anxiety, pain acceptance and determined resilience were concerned, mediating the effect between these factors and pain intensity, life interference, pain-related distress, life control and the degree to which activities had been

reduced by pain (MPICb). When mediated by pain catastrophising, acceptance and resilience both predicted decreases in pain intensity, life interference, distress and the MPICb and an increase in life control, indicating that when resilience and pain acceptance result in less catastrophic thinking, pain outcomes improve.

It was reported earlier, in the discussion of the regression analysis (Section 11.2.2), that acceptance and determined resilience did not predict pain intensity, determined resilience contributed to a small amount of variance in life interference, and determined resilience and the sub scale of acceptance, activity engagement, contributed to the prediction of greater pain-related distress. The difference in these results can be explained by the presence of a mediator, in this case pain catastrophizing. Pain acceptance did not have a direct effect on any of the pain outcomes other than pain intensity, suggesting that pain catastrophizing is likely to be the only mediator, supporting this theoretical framework. Where pain intensity is concerned, as acceptance had a direct effect as well as an indirect mediated effect it suggests that there is likely to be an additional mediator that has been omitted in this model. Determined resilience had direct effects, in addition to mediated effects on distress and life control, again suggesting that mediators other than just pain catastrophizing might be present. For pain intensity, life interference, and the MPICb it is likely that pain catastrophizing is the only mediator as no direct effects of resilience were found.

Where pain acceptance is concerned, and in contrast to this study, previous research has found that acceptance directly predicts various pain-related outcomes, such as reduced pain intensity, physical disability and pain-related distress, and improved physical functioning in the able-bodied (McCracken & Gutierrez-Martinez, 2011; McCracken & Eccleston, 2003) and spinal cord injured populations (Kim, Williams, Hassett, & Kratz, 2019; Jensen et al., 2016). This was without the presence of an identified mediator. However the mediation model in this study did not show a total effect on any of the pain outcomes other than ‘support’. All other effects were mediated by pain catastrophizing. These results suggest that pain catastrophizing has an

important role in the relationship between acceptance and pain and supports previous research which found that acceptance is both correlated with and predicts catastrophic thinking (Gillanders, Ferreira, Bose & Esrich, 2012; De Boer, Steinhagen, Versteegen, Struys, & Sanderman, 2014).

It has been suggested that higher pain acceptance increases engagement in valued activities and reduces fear-avoidance, which in turn reduces catastrophic thinking (Crombez, Eccleston, Van Damme, Vlaeyen & Karoly, 2012; Ramírez-Maestre, Esteve & López-Martínez, 2014). This then leads to the better pain-related outcomes found in this study. This effect could be magnified for people with SCI because if the individual is experiencing difficulties with activity engagement, this could disrupt the processes of rehabilitation and adaptation. Additionally, Craner, Sperry, Koball, Morrison, and Gilliam (2017) have suggested that acceptance and pain catastrophizing act on pain outcomes in different ways. Acceptance has a greater impact on physical functioning, whereas pain catastrophizing affects pain intensity and distress (Craner et al., 2017). The results of the multiple regression analysis reported earlier support this to a degree, finding that catastrophizing predicted pain intensity, and acceptance predicted life interference from pain, but also increased pain-related distress. What is clear is that the combination of the two therefore, can have a far reaching impact on a range of outcomes, a suggestion supported by these results.

Pain catastrophizing also mediated the relationship between determined resilience associated with appraisal of injury and many pain-related outcomes. As was the case with pain acceptance, outcomes associated with pain improved when higher resilience resulted in lower catastrophic thinking. That both resilience and pain acceptance have similar effects when mediated by pain catastrophizing supports earlier research identifying a strong relationship between the two (Ramírez-Maestre, Esteve, & López-Martínez, 2014). Where determined resilience is concerned, this result is unsurprising as resilience has been associated with lower catastrophic thinking (Ong, Zautra & Reid, 2010), and lower catastrophic thinking has been associated with better pain outcomes, both in this study and in previous research (Kim, Williams, Hassett,

& Kratz, 2019).

The mediated effect of resilience on pain outcomes found here, provides evidence in support of Sturgeon and Zautra (2010), who proposed a model of 'pathways to resilience' for people with chronic pain conditions (see Section 4.3). This model suggests that people have both trait resilience and vulnerability traits. When pain flares up, vulnerability traits such as depression and childhood trauma can lead to vulnerability mechanisms, one of which is pain catastrophizing. However trait resilience can lead to the utilisation of resilience resources, such as social support and positive coping strategies. If resilience resources are high these can reduce the extent of vulnerability mechanisms, resulting in, for example, less catastrophic thinking and leading to recovery and growth (Sturgeon & Zautra, 2010). For people with SCI, if resilience reduces pain catastrophizing resulting in better pain-related outcomes, as suggested by this study, the chances of achieving recovery and growth are magnified. Duggan et al. (2016) suggest that resilience is a key facilitator in adapting to injury, and resilience resources, as proposed by Sturgeon and Zautra (2010), can be developed. This further strengthens the notion that the development of resilience needs to be part of rehabilitation programmes. If it was, then higher resilience and the resulting lower pain catastrophizing would be instrumental in leading to positive adaptation and adjustment.

The effect of anxiety on pain-related outcomes was also mediated by pain catastrophizing. Anxiety, however, had the opposite mediated effect to acceptance and resilience, increasing pain intensity, life interference, distress and the MPICb, and reducing life control. As well as the mediated effects, direct effects were also found on life interference, pain-related distress, and life control. This suggests that pain catastrophizing is not the only variable to have a mediating role on these outcomes and that additional mediators are likely to be involved. However, only indirect effects were found on pain intensity and the MPICb indicating that the theoretical framework is likely to be accurate and pain catastrophizing is the only mediator here. Perceived stress also increased pain intensity, life interference, life control and the MPICb when

mediated by pain catastrophizing. However, it did not have a mediated effect on distress, although it did directly influence it, as discussed earlier, which might mean that a different mediator is involved.

It was noted earlier that anxiety did not contribute to the prediction of any of the pain outcomes when entered in a regression model. These results suggest that rather than having a direct impact, the effects of anxiety are mediated by pain catastrophizing, once again implicating catastrophic thinking as highly influential in peoples' pain experience. This supports Ullrich, Jensen, Loesser and Cardenas (2007) who found that catastrophic thinking mediated the relationship between distress and pain outcomes. Additionally, Craig et al. (2017) have associated anxiety with more catastrophizing and higher ratings of pain intensity. This is important because it has been widely reported that anxiety and pain catastrophizing have a much greater negative impact on quality of life than the pain itself (Müller et al., 2017; Richardson et al., 2016; Wollaars, Post, van Asbeck and Brand, 2007). One facet of anxiety that might be key here is worry. The MPM (Eccleston & Crombez, 2007) suggests that worry is central to individuals getting stuck in the perseverance loop of repeated attempts to solve the problem of pain that ultimately fail. The worry about the pain, driven by the implications it has for participation in valued activities, leads to greater attention being paid to it in the form of hypervigilance. This could take the form of pain catastrophizing as suggested by this study. For people with SCI the worry about the impact of pain is likely to be greater, given that failure to engage in activities results in poorer rehabilitation outcomes. Worry about the consequences, therefore, will lead to further catastrophic thinking, and the negative outcomes suggested by these results. This is partially supported by the fact that in the regression analysis, magnification (a sub scale of pain catastrophizing) predicted life interference from pain. The mediation analysis builds on this to indicate that anxiety combined with the mediation of catastrophic thinking results in much broader negative consequences.

Depression and negative appraisal of injury did not directly affect pain intensity, but they did indirectly via the mediator of catastrophic thinking (as

these two predictors increased, pain increased), again implicating catastrophic thinking as an influential negative psychological variable where pain outcomes are concerned. Negative appraisal of injury did not have a mediated effect on any of the other pain outcomes but it did have a direct effect on life interference, distress, life control, and the MPICb, which suggests that other mediators might be involved. Also, as discussed below, appraisal of injury emerged as an important mediator between the other biopsychosocial variables and pain outcomes, suggesting its influence may be stronger in that role.

Depression and mental defeat both had a positive indirect effect on the MPICb, signifying that as these two predictors increase, resulting in higher catastrophic thinking, people are more likely to reduce the activities they would normally engage in, because of their pain. As no direct effects were found between these two predictors and the MPICb it is unlikely that other mediators are involved. Consistent with this, higher mental defeat also predicted greater life interference from pain when mediated by catastrophizing, again with no direct effect suggesting pain catastrophizing is the only mediator. This is in line with the theory of the Involuntary Defeat Strategy (Sloman, 2000), which suggests that as competition for resources increases, activity towards goals that are perceived as unachievable reduce as a way to minimise costs. Sloman (2000) explains the association between mental defeat and depression by suggesting that when the Involuntary Defeat Strategy is inappropriate, it results in psychological disorders such as depression. Where SCI is concerned, the competition for resources might reflect an individual's physical resources, which limit the amount the person can do. When the individual perceives that they cannot achieve all they want to, it might result in mental defeat and depression, leading to the reduction in engagement in activities seen in the results of this mediation analysis.

Taylor, Gooding, Wood and Tarrier (2011) suggest that in humans this sense of defeat might stem from loss or failure in a wide range of goals; it is likely to be even greater with the addition of a SCI and pain, which inevitably result in losses of, for example, the ability to do the things they used to or the role they

had in the family or workplace (Dickson, Allan, & O'carroll, 2008). Because the losses are perceived as significant, pain catastrophizing increases, mediating the effects of mental defeat and depression, and resulting in greater life interference. Tang, Goodchild, Hester and Salkovskis (2010) have associated this to the MPM. They suggest that as people repeatedly try to solve the problem of pain in order to minimise the losses, and to make the most of the physical resources they have available, they experience a greater sense of defeat, and are more likely to become stuck in the perseverance loop. For people with a SCI this might result in reduced efforts to engage in activities that could cause pain and limit their resources even further, and ongoing efforts to solve the pain. In this way, as this study has found, mental defeat and depression, mediated by catastrophic thinking lead to a reduction in activities and greater life interference because of the pain.

Pain catastrophizing did not mediate the effects of significant others' responses on any of the pain outcomes. A distracting response and a solicitous response both had a direct effect on support in that as this type of response increased, so did the perception of support. A negative response had a direct effect on life interference and distress which similarly showed that an increase in negative responses predicted an increase in these pain outcomes, supporting the results of the regression analysis discussed earlier. Given these results, it is likely that another mediator might be involved but that catastrophic thinking is not involved as a mediator where another's response is concerned. The fact that solicitousness had a positive direct effect on support reinforces the suggestion that for people with a SCI, solicitousness is perceived as being helpful. This is in contrast to the able-bodied literature which has associated solicitousness with negative outcomes, such as increased disability and poorer functionality (Hemphill, Martire, Polenick, & Parris Stephens, 2016). As discussed earlier, it is likely therefore, that solicitousness enables people with SCI to engage in activities and work towards independence.

In general, however, the results of these mediation analyses suggest that the way a significant other person responds to an individual in pain does not have

the influence on pain outcomes that has been found in previous research. For example, increased pain has been associated with solicitous and negative responses (Pow, Stephenson, Hagedoorn, & Delongis, 2018), and greater distress and depressive symptoms have been associated with negative and distracting responses (Stroud, Turner, Jensen, & Cardenas, 2006). It is possible that other mediators are involved and that the effects of others' responses are not apparent because of this. Alternatively, it might be that rather than being the predictors of pain outcomes, the way someone responds has a more influential role as a mediator. This has been suggested previously in the wider health literature by Slatcher and Schoebi (2017) who found that partner responses mediated the effect of close relationships on health more broadly. It is quite possible that they may also mediate the effects of psychological variables on specific pain outcomes. Further research is necessary to determine whether this is the case.

11.5.2 Pain acceptance as a mediator

It was anticipated that pain acceptance would also emerge as a key mediating variable between biopsychosocial predictors and the seven pain outcomes. However, with acceptance as the mediator, there were only significant indirect effects between pain catastrophizing, mental defeat and stress and the pain outcome 'support'. In contrast, the various psychosocial factors predicted many of the pain outcomes directly, without the mediating role of acceptance, suggesting that other mediating variables are likely to be involved. These results support Elvery, Jensen, Ehde, and Day (2017) who found that pain catastrophizing was a more important predictor and mediator of pain intensity and pain interference than acceptance. As discussed above, the results of this study found that pain catastrophizing mediated the effects of many of the variables measured on pain outcomes. However, it is in contrast to Vowles, McCracken and Eccleston, (2008) who suggested that acceptance might be an important meditator between psychological variables, such as pain catastrophizing, and various pain-related outcomes.

It is important to note though that Vowles et al. (2008) were focused on able-

bodied people with pain and, as has already been discussed, this study has highlighted some key differences in the way pain acceptance influences pain outcomes in the able-bodied and spinal cord injured populations. It is possible that for people with SCI, rather than mediating the effects of various factors on pain outcomes, pain acceptance is a predictor of those outcomes. In this study, when mediated by pain catastrophizing, acceptance predicted pain intensity, life interference, pain-related distress, life control and the degree to which pain reduced activity engagement. Additionally, when appraisal of injury was analysed as the mediator (see discussion below), pain acceptance predicted pain-related distress and life control, but also activity engagement more generally. This supports the idea that in people with SCI, pain acceptance is an important predictor of pain outcomes rather than being a mediator.

It is also possible that pain acceptance influences pain in ways not analysed in this study. For example, there is a strong relationship between acceptance and depression (Costa & Pinto-Gouveia, 2013), acceptance has been found to predict depression over time (Pinto-Gouveia, Costa & Marôco, 2013), and it has been found to mediate the effects of pain on depression (Pinto-Gouveia, Costa, & Marôco, 2016). This suggests that as well as impacting on the pain outcomes measured in this study when mediated by pain catastrophizing and injury appraisal, acceptance may have a greater influence on the psychological consequences of pain. This idea has been supported longitudinally where pain acceptance has mediated the effects of Cognitive Behavioural Therapy programmes on depressive symptoms (Baranoff, Hanrahan, Kapur & Connor, 2013; Akerblom, Perrin, Fischer & McCracken, 2016), even when pain intensity and pain catastrophizing were controlled for (Baranoff et al., 2013).

Studies focusing on acceptance in the spinal cord literature have also associated acceptance and depression, with greater acceptance predicting reduced depressive symptoms and negative affect (Jensen et al., 2016; Kratz, Hirsh, Ehde & Jensen, 2013). It is likely, therefore, that acceptance exerts its influence on emotion regulation, which concurs with Kohl, Rief and

Glombiewski (2012) who found that, where pain is concerned, emotion regulation is more effective when acceptance strategies are utilised. It is also consistent with the regression analysis discussed earlier, which found that pain acceptance predicted pain-related distress, but not pain intensity or life interference from pain. Although, here, greater pain acceptance in the form of activity engagement, predicted higher distress. As stated earlier, it is possible that this forms a key stage in the process of achieving pain acceptance. The association between acceptance and psychological distress might explain why the two processes of increasing independence and an evolving pain view are deemed to be so important to Henwood et al's (2012) model depicting how people with SCI move forward with their pain. Depression and low mood are often associated with a negative bias (Beck, 1979). If acceptance of pain is low early on resulting in low mood, it is likely that people will view their degree of independence negatively and find it more difficult to change their pain view, hampering their ability to integrate pain into their lives, the final stage in the model. This in turn would maintain low pain acceptance. Further research is necessary to clarify the impact of acceptance on depression for people with SCI and to determine whether such a reciprocal relationship exists.

In summary, pain acceptance did not emerge as an important mediator between the biopsychosocial variables and pain outcomes. Two possible explanations are proposed as to why this might be. Acceptance might have a greater influence on the psychological consequences of pain, mediating the relationship between pain and depression, or more generally, between pain and emotion regulation. Additionally, pain acceptance might be a better predictor of pain outcomes when mediated by other factors, rather than being a mediator. This latter proposal is supported by the results of the mediation analyses in this study, where pain catastrophizing and appraisal of injury were found to mediate the relationship between pain acceptance and a range of pain outcomes. Further research is necessary to explore whether pain acceptance is equally influential in predicting or mediating the relationship between pain and its psychological consequences.

11.5.3 Appraisal of injury as a mediator

Catastrophic negativity and determined resilience (as types of injury appraisal) were also analysed as mediators to explore how an individual's appraisal of their SCI might impact on, or interact with, their pain experience. When initially analysed as predictors, catastrophic negativity only had an indirect effect on pain intensity when mediated by pain catastrophizing and neither catastrophic negativity or resilience had any indirect effects on any pain outcomes when mediated by pain acceptance. It was therefore considered that they might have more influence in a mediating role. This was found to be the case; appraisal of disability had a mediating effect between most psychosocial factors and pain outcomes. The only two factors whose effects were not mediated by appraisal of disability were cortisol concentration (which effects had previously been found to be mediated by catastrophic thinking) and a solicitous response from a significant other person. The majority of factors indirectly affected the pain outcomes when mediated by catastrophic negativity and resilience in combination, and also when mediated by each of these individually. The only instance where this was not the case was pain acceptance where there was a mediating effect of both types of appraisal combined and of determined resilience on its own, and a distracting response from a significant other person where only determined resilience had a significant mediating effect.

The role of appraisal of injury as a mediator was particularly influential in the relationship between most predictors and pain outcomes. For the predictors stress, pain catastrophizing, anxiety and a negative response from a significant other, injury appraisal predicted the following six of the pain outcomes: life interference, pain-related distress, support, life control, activity engagement (MPICa) and the degree to which activity engagement has been reduced because of pain (MPICb). Injury appraisal mediated the effects of mental defeat on all of these pain outcomes apart from support, on which it had no direct or indirect effect. The effects of depression were mediated on all of these pain outcomes apart from the MPICb.

Interestingly, appraisal of injury did not mediate the effect of any of the predictor variables on pain intensity. Pain catastrophizing has emerged as a more prominent mediator in this respect, influencing the relationship between all of these predictors, apart from mental defeat, and pain intensity ratings. Research in SCI has not looked at appraisal of injury and its relationship to pain. However, in the broader pain literature, general resilience has been associated with the use of effective coping strategies, a more positive attitude towards pain and better adjustment to chronic pain conditions (Sturgeon & Zautra, 2010; Ramírez-Maestre, Esteve, & López-Martínez, 2014). It has not specifically been associated with the severity of pain. This is in contrast to pain catastrophizing, which has been associated with a range of pain outcomes, including pain intensity, in the able-bodied pain population (Vase et al., 2011; Craner, Gilliam and Sperry, 2016).

Whilst an association between pain catastrophizing and pain intensity has not always been found in SCI research (Finnerup et al., 2016), it has been found in some studies (Nicholson Perry, Nicholas & Middleton, 2009). An explanation for this disparity might be that, rather than directly predicting pain ratings, pain catastrophizing has a more influential role as a mediator between other variables and pain intensity. The results of this study support this and go further to indicate that whilst injury appraisal and pain catastrophizing combine to mediate the effects on a range of pain outcomes, pain catastrophizing alone has this role where pain intensity is concerned. One reason for this could be the association that pain catastrophizing has with pain modulation systems. Weissman-Fogel, Sprecher and Pud (2008) suggest that catastrophic thinking reduces the diffuse noxious inhibitory control mechanism, which reduces the activity of neurons sending pain messages in the dorsal horn of the spine, allowing for an amplification of those pain signals. Additionally, Seminowicz and Davis (2006), have found that catastrophic thinking activates areas in the brain, such as the dorsolateral prefrontal cortex and the insula, which are associated with affective aspects of pain and attention. This they suggest, could represent a pain vigilance system. Therefore, pain catastrophizing might be an important mediator between psychological variables and pain intensity because it modulates pain inhibitory mechanisms and increases attention to

pain (Weissman-Fogel, Sprecher and Pud, 2008; Seminowicz and Davis, 2006). This provides additional support for the biopsychosocial model, suggesting a biological route by which pain catastrophizing mediates the effects of other variables on pain intensity.

With regards to all of these six predictor variables (stress, mental defeat, pain catastrophizing, anxiety , depression and negative responses from others), determined resilience and catastrophic negativity had slightly different mediating effects. The model with both mediators predicted life interference, distress, and life control. Catastrophic negativity contributed to these mediations but also mediated the effect on the degree to which pain reduced activity engagement (MPICb). Resilience mediated the effects on distress and life control, but not on life interference or the MPICb. However it additionally mediated the effect on the MPICa and support. This suggests that whilst both types of appraisal have an impact on certain pain outcomes, negative appraisals have a greater mediating influence on reductions in physical functioning due to pain and on life interference, and resilience has a greater mediating influence on activity engagement and on the amount of support an individual in pain will receive. This latter result supports the notion discussed earlier that solicitous responses from a significant other may reduce over time because of carer burnout (Newton-John, 2013; Cano et al., 2012). If the individual in pain demonstrates determined resilience regarding their SCI, it may be easier for those around them to continue providing support. Early studies have found similar results in the pain population, with the degree of depressive symptoms experienced by a spouse of someone in pain being determined by how well the person in pain is coping (Feinauer & Steele, 1992). This implies therefore, that these predictors, mediated by a positive appraisal of injury not only have a positive effect on pain outcomes, but also on social support, a key factor in successful adaptation to injury.

As just stated, a negative appraisal of injury mediates the effects on life interference and the degree to which activity engagement is reduced by pain. In contrast, determined resilience mediates the effects on support and activity engagement. Therefore, when an individual receives negative responses from

others or they have high catastrophic thinking, mental defeat or stress, and they appraise their injury negatively, it is most likely to result in poorer functional outcomes in the form of greater life interference and a reduction in activities of daily living due to the pain. However, if they appraise their injury positively it is likely to result in greater activity engagement. This suggests that a negative injury appraisal has a more effective mediating effect on the negative functional outcomes, and resilience is more influential with regards to the more positive functional outcomes. This supports previous longitudinal studies, which have found that negative appraisals of injury predict poorer functional outcomes (Kennedy et al., 2010) whereas resilience predicts a much lower likelihood of developing a psychological disorder (Craig et al., 2015). If people are psychologically more resilient they are more likely to have the motivation and desire to engage in activities. Given that the type of appraisal made acts on different pain outcomes, pain management programmes which only attempt either to reduce negative cognitive appraisals or to develop resilience will only be targeting specific aspects of pain and improvements will not be seen across all of its consequences. It is important therefore to include both positive and negative predictors of pain outcomes in such programmes.

Where pain catastrophizing is concerned, the results of this study suggest that there is a reciprocal mediating relationship between appraisal of injury, particularly determined resilience, and catastrophic thinking. Earlier it was reported that pain catastrophizing mediated the relationship between resilience and pain intensity, life interference, distress, life control and the MPICb. In this analysis injury appraisal was found to be the mediator between pain catastrophizing and pain outcomes. It is possible that greater determined resilience in terms of injury appraisal leads to lower catastrophic thinking and the beneficial pain outcomes identified earlier, but that these improved pain outcomes then result in further reductions in catastrophic thinking and continuing positive appraisal of injury, manifesting as resilience. This would support Duff and Kennedy, (2003) who suggested that appraisal of injury continues beyond the initial acute stages, and changes in line with the new information received. Also, Dean and Kennedy, (2009) found that injury

appraisal influences coping strategies, but that the coping strategies then go on to influence how the injury is perceived. Pain catastrophizing can be considered to be a negative coping strategy (Sullivan, 2012). These studies support the idea that injury appraisal and pain catastrophizing may continue to influence each other so that both may be predictor and mediator of the other, as has been found in this research.

In the discussion of pain catastrophizing as a mediator, it was highlighted that some of the variables had direct effects as well as, or instead of, indirect effects, indicating that an additional mediator is involved. In the case of stress, anxiety, depression and negative responses from others, in every instance where they directly affected pain outcomes, an indirect effect was found in the analysis where injury appraisal was the mediator. This suggests that pain catastrophizing and injury appraisal combine to mediate the effects of a number of psychological factors on a range of pain outcomes. However, where pain acceptance was concerned this was not the case. Acceptance had a direct effect on pain intensity and support in the analysis with catastrophizing as mediator, but appraisal of injury did not mediate these relationships. Similarly, both distracting and solicitous responses had direct effects on support which were not mediated by either pain catastrophizing or appraisal of injury. This suggests that additional, as yet unidentified mediators are involved, providing further evidence of the complexity of the pain experience.

Where the responses of a significant other are concerned, appraisal of injury was more influential in the relationship between them and the pain outcomes than was pain catastrophizing. As well as mediating the effects between negative responses and the six pain outcomes mentioned earlier, injury appraisal also mediated the effect of a distracting response on pain-related distress, life control and activity engagement (MPICa). It did not mediate the effect between solicitousness and any of the pain outcomes. However, where distracting responses are concerned, it was only determined resilience that was influential. Neither catastrophic negativity nor the two appraisal types combined had a mediating role.

This suggests that determined resilience is a particularly important type of injury appraisal where a distracting response is concerned. As distracting responses increased, so did resilience, resulting in less pain-related distress, an increased sense of control and greater engagement in activities. In the regression analysis discussed earlier, more distracting responses from significant others predicted greater life interference, which is at odds with this mediation result. Here, there was no indirect effect on life interference although there was a direct effect which, consistent with the regression analysis, suggests that as distracting responses increased, so did life interference. This indicates that a different mediator is likely to be involved in that relationship. It also adds weight to the importance of determined resilience in the relationship between social responses and pain outcomes. If people are appraising their injury with resilience the consequences of a distracting response will be better in terms of the level of distress an individual feels, the degree of control they perceive they have and the activities they will engage in. Without determined resilience, a distracting response has a more negative effect in terms of increased life interference.

This can be partially explained by Turk and Kerns's (1985) Transactional Model of Health which suggests that whilst the way the family responds to an individual in pain is important, the way the individual perceives that response is particularly influential on the outcome. With regards to these results, an individual who demonstrates determined resilience with regard to their SCI may be more likely to appraise a distracting response from a significant other as positive and enabling rather than an interference. The model also explains why a distracting response predicted increased life interference on the one hand whilst concurrently, the mediated effect improved activity engagement and a sense of control.

Turk and Kerns (1985) acknowledge that the same response from a family member may impact on one dimension in one way, whilst affecting a different dimension in another way. This would suggest that distracting responses, coupled with resilience, may encourage someone to engage in certain activities of daily living, or in hobbies and interests, which improves the

individuals perception of control and reduces distress, but also is viewed as an interference. In this way it is conceived that in determining the consequences on pain outcomes, the way the response of a significant other is appraised by the individual in pain, is as important as the response itself, and that same response might impact on the different outcomes in different ways (Lewandowski, Morris, Draucker, & Risko, 2007). As suggested earlier, further qualitative research is needed to determine how individuals with SCI perceive responses from other people and the impact it has on their pain experience.

11.5.4 Further mediation analysis of the relationship between stress and cortisol

Stress and cortisol are closely linked but this study did not find a relationship between them. To explore the relationship further, additional mediation analyses were undertaken using cortisol as a mediator between stress and the pain outcomes, and then using stress as the mediator between cortisol and the pain outcomes. There were no significant indirect effects in any of these analyses suggesting that these two variables do not mediate the effect of the other on pain outcomes. Catastrophic thinking and appraisal of disability were found to be more influential as mediators between cortisol and stress and the various pain outcomes.

In general, whilst both mediators have been found to be influential in this study, appraisal of injury was found to be a more important mediator between biopsychosocial factors and pain outcomes than pain catastrophizing. Injury appraisal mediated the effects of stress, mental defeat, anxiety, depression, and negative and distracting responses on more pain outcomes than pain catastrophizing. Pain catastrophizing, however, was more influential as a mediator than injury appraisal where pain acceptance and cortisol were concerned, being the sole mediator between cortisol and pain outcomes, and mediating the effect of acceptance on a wider range of pain outcomes than appraisal of injury. Pain acceptance did not emerge as an important mediator and it is speculated that it may have greater influence as a predictor.

These results suggest that both pain catastrophizing and appraisal of injury combine to influence the effects of various biopsychosocial factors on a wide range of pain outcomes for people with SCI. This supports much of the literature where pain catastrophizing is concerned (e.g. Kim, Williams, Hassett, & Kratz, 2019; Craig et al., 2017). However, it is the first time that the way an injury is appraised has been directly associated with pain outcomes for people with SCI. It highlights the fact that injury appraisal has greater prominence than just predicting psychological and physical functioning outcomes following such an injury, but that cognitive appraisals also have a wide ranging impact on pain outcomes. These results, therefore, identify an important link between appraisal of disability, catastrophic thinking and pain, providing further information about the interaction between them.

11.6 **Psychosocial predictors of appraisal of injury**

During the mediation analysis it was noted that many of the psychological and social variables had a significant effect on the way individuals appraised their disability in terms of catastrophic negativity or determined resilience. The final analysis of the study explored which factors specifically might be influential. Pain catastrophizing, mental defeat, pain acceptance, anxiety and perceived stress in combination predicted both types of appraisal. Pain catastrophizing, anxiety and mental defeat all predicted higher catastrophic negativity, whereas pain acceptance predicted greater resilience and perceived stress predicted lower resilience. The responses of a significant other person to the individual in pain (distracting, negative or solicitous) did not significantly predict catastrophic negativity but they did predict resilience. A distracting response predicted an increase in resilience and a negative response predicted reduced resilience. This indicates that both psychological and interpersonal factors can be influential in the way appraisals of disability are made, as well as having an impact on pain outcomes.

In the SCI literature, studies have focused on how appraisal of injury might predict psychological wellbeing, adaptation and functional outcomes (Mignogna, Christie, Holmes & Ames, 2015; Kennedy et al., 2010) rather than

exploring what might predict the way in which someone appraises their injury. Given that this study has demonstrated the importance of injury appraisal as a mediator where pain is concerned, understanding what might predict the type of injury made is very relevant to the effectiveness of rehabilitation services and pain management programmes. Of additional consideration is that appraisal of injury has been found to predict outcomes such as depression and anxiety (Eaton, Jones & Duff, 2018; Mignogna, et al., 2015; Kennedy Evans & Sandhu, 2009), and this study has found that these factors also predict appraisal of injury. This suggests that there may be a reciprocal relationship, with various factors predicting how an individual will appraise their injury, and the injury appraisal then going on to predict ongoing difficulties with, for example, depression and anxiety. The way this may work could be through the pain outcomes that are mediated by injury appraisal and catastrophic thinking. When pain outcomes are negative it might lead to greater anxiety, depression and mental defeat for example. This supports Duff and Kennedy (2003) and Dean and Kennedy (2009) who have both implied that there may be a circular relationship between injury appraisal and certain other factors, with additional information continuing to influence the type of appraisal made beyond the acute stages. Further research is need to explore the possible reciprocal relationship between injury appraisal and the other factors considered in this study to see whether such a relationship exists and to explore the contribution that pain might make.

In summary, the results of this final part of the analysis provides a clearer picture of how psychosocial variables impact on appraisals of disability, which in turn mediates the effect on pain outcomes.The problem of pain should not, therefore, be treated solely with an understanding of an individuals cognitions regarding their pain, but also with an understanding of their cognitions regarding their disability.

12 Chapter 10 - General Discussion

The purpose of this study was to see how a range of biopsychosocial variables interact to influence the pain experience for people with SCI. From the results obtained, a number of key outcomes have emerged. These outcomes have been extracted from the discussion above, and will now be highlighted within the framework of the biopsychosocial model.

12.1 Key Biological Outcomes

Cortisol did not emerge as an influential predictor of pain outcomes on its own. However, in combination with pain catastrophizing, it was revealed to be more influential than at first thought. Pain catastrophizing mediated the effects of cortisol on pain intensity, life inference, pain-related distress, life control, activity engagement, and also depression, demonstrating a very strong association between the two, and providing evidence for the route through which cortisol impacts on the pain experience. This supports Melzack (2005) who proposed that the link between cortisol and pain conditions could be certain psychological factors. It also adds additional evidence of the association between catastrophic thinking and the neural mechanisms of pain (Weissman-Fogel, Sprecher & Pud, 2008; Seminowitz & Davis, 2006). This implies that the role cortisol plays in the pain experience cannot be considered in isolation from other psychological variables, specifically catastrophic thinking. When mediated by pain catastrophizing, the effects of cortisol go beyond just pain intensity, to impact on a wide range of pain outcomes, including depression, verifying the important influence of this biopsychological combination.

An additional point to note about cortisol was the way in which it reduced over time. It is unclear whether the reduction of cortisol over time reflects a healthy return to premorbid levels or hypocortisolism. Given its close association with pain catastrophizing, which worsened over time in this study, it is possible that it reflects the latter. This gives cause for concern as hypocortisolism has a negative impact on immune functioning (Fries, Hesse, Hellhammer, &

Hellhammer, 2005), and the risk of infection is high and particularly problematic for people with SCI. It is possible, therefore, that cortisol and pain catastrophizing is a particularly toxic combination for people with SCI and pain.

12.2 Key Psychological Outcomes

12.2.1 Poorer psychological outcomes over time

A clear outcome of this study has been the indication that as people with SCI and pain transition into the community following rehabilitation, their psychosocial outcomes worsen. This was found at a number of different stages of the analysis. Where the comparison between in-patients and out-patients was concerned, the out-patient group appraised their disability far more negatively, showing lower determined resilience and higher catastrophic negativity than the in-patient group. Additionally, the out-patient group displayed lower pain acceptance and received fewer solicitous responses from a significant other. In the longitudinal study in-patients at time three, when the majority had been discharged from hospital, had increased levels of depression and pain catastrophizing in the form of magnification, and lower determined resilience concerning injury appraisal, in relation to in-patients at time one. When the biopsychosocial factors were correlated with time since injury, mental defeat and helplessness, (a sub scale of pain catastrophizing), both increased with time. These results clearly demonstrate that rather than adjusting to the injury and seeing an improvement over time, a significant number of people with pain experience a worsening of an important range of these psychosocial variables. This supports Craig et al. (2017) and Bonanno et al. (2012) who both found that for a significant minority of people psychological well-being reduced once they had left hospital.

As has been discussed earlier, this might reflect the fact that less professional support is available once people are living back in the community (van Loo et al., 2010) and that the support available may be from people who are not specialists in SCI (Cox, Amsters, & Pershouse, 2001; Neri & Kroll, 2003). These results might also reflect a masking of problems whilst the person is in

hospital receiving intensive treatment, which only emerge once the individual is back in the community. At this stage, people may view the challenges associated with their injury as more threatening once they are dealing with them on their own (Eaton et al., 2018; Bonanno et al., 2012). Additionally they may become more aware of the losses that are the consequences of the injury, for example, losses in status, employment, role in the family, and financial losses (Martz et al., 2005). This is important because of the negative impact these problems have on adjustment and adaptation to injury.

12.2.2 The role of acceptance in SCI

It has become apparent that pain acceptance presents different challenges for people with pain and SCI than for those in the able-bodied population. The results of the in-patient and out-patient comparison study found that pain acceptance was lower for out-patients. Additionally the multiple regression analysis found that activity engagement, a sub scale of the CPAQ, predicted increased pain-related distress, rather than an improvement as might have been expected. These two sets of results imply that pain acceptance is difficult for people once they have left hospital, and that engaging in activities without the support of health professionals can result in greater distress. It is speculated that this might be because the SCI provides greater challenges in activity engagement, with pain making it harder to persevere with goals of independence (Gruener et al., 2018). However, disengaging from the goals when they feel unattainable is not always possible when they are necessary in the adaptation to the SCI. Solving the problem of pain becomes important therefore, if independence is to be achieved. In contrast to the able-bodied pain population this is an important stage that people with SCI must go through to reach the point of being able to live well with pain (Henwood et al., 2012). This supports previous research which has found that staying in the present moment, which is part of mindfulness training and a facet of pain acceptance, results in greater distress when SCI and pain are present (Dorado et al., 2018). Instead, focusing on the future, with the hope of independence, increases resilience (Sparkes & Smith, 2008). This in turn might enable greater engagement in activities that help the individual move towards that

goal, despite the distress it may cause.

Further evidence that pain acceptance operates differently for people with SCI is that, in contrast to studies in the able-bodied population (Vowles et al., 2008), pain acceptance did not emerge as an important mediator between psychosocial variables and pain outcomes. It was far more influential as a predictor of pain outcomes, mediated by pain catastrophizing and injury appraisal. Additionally, given that acceptance predicted greater distress in the regression analysis, it might be that it is more likely to mediate the effects of pain on its psychological consequences, such as depression, as suggested by Pinto-Gouveia et al. (2016).

12.2.3 The important influence of pain catastrophizing

Pain catastrophizing emerged as a particularly important psychological variable with regard to the consequences of pain and SCI. When all three sub scales of catastrophizing were entered into a regression model with stress, increases in pain intensity, interference from pain and pain-related distress were predicted. Pain catastrophizing was particularly influential where pain intensity and pain interference were concerned suggesting that it affects both sensory and functional aspects of pain. This is of interest because in the regression analysis pain intensity was not widely predicted, with pain catastrohizing being the only contributing variable. However, with catastrophizing as a mediator, the majority of the variables, apart from mental defeat and the responses of others, affected pain intensity, indicating that catastrophic thinking has an important role where the severity of pain is concerned. This supports studies that have associated catastrophic thinking with a reduction of activity in inhibitory pain mechanisms (Weissman-Fogel et al., 2008; Seminowicz and Davis, 2006). Such studies provide an explanation for the results found here and further demonstrate the close link between pain catastrophizing and the biological factors associated with pain.

Whilst pain catastrophizing predicted pain intensity and pain interference in the

regression analysis, its role as a mediator had more far reaching effects, mediating the effects of all the other variables, apart from the responses of others, on a wide range of pain outcomes. The results of this study also suggest that pain catastrophizing has a reciprocal relationship with the way an individual appraises their injury. Catastrophic thinking mediated the effects of injury appraisal, particularly determined resilience, on a number of pain outcomes. Injury appraisal, however, also mediated the effects of pain catastrophizing on the consequences pain. It is possible that a more negative appraisal of the SCI generates greater catastrophic thinking, and that this in turn leads to ongoing negative injury appraisal. This supports Duff and Kennedy (2003) who suggested that appraisals continue beyond the acute stages, changing as people are faced with new challenges. Importantly, the combination of the two result in poorer pain outcomes, potentially undoing the gains made during rehabilitation and hampering successful adaptation to the injury.

Over all the results of this study identify catastrophic thinking as a key factor in the experience of pain for people with SCI. It links both biological and psychological factors with the consequences of pain and is also associated with the cognitive appraisal of injury. Ultimately, this determines how severe those pain outcomes will be.

12.2.4 Pain and the appraisal of SCI

Of all the variables measured in this study, appraisal of injury had the most far reaching effects. As already stated, out-patients appraised their SCI with greater negativity than in-patients, demonstrating lower determined resilience. However, of particular interest is the association between the way in which an individual appraised their injury and their pain experience. In the regression analysis, a negative appraisal of the injury predicted increased interference from pain and greater pain-related distress. In contrast, a positive appraisal predicted less pain interference and lower distress associated with pain. This signifies that the way an injury is appraised has a direct effect on both affective and functional consequences of pain. This is in contrast to pain

catastrophizing, which predicted sensory and functional pain outcomes. The combination of the two, therefore, impact widely on peoples' pain experience.

Appraisal of injury also emerged as an influential mediator between most of the other variables, apart from solicitous responses and cortisol, and a wide range of affective and functional pain outcomes. It did not mediate the effects of any variable on pain intensity. It appears from these results that pain catastrophizing has a closer association with the biological underpinnings of pain than injury appraisal. However, in all other respects appraisal of injury was an even stronger mediator than pain catastrophizing, mediating the effects of both psychological and social variables. This is a particularly important result as the association between injury appraisal and the pain experience has not been examined before. Previously, it has been associated more generally with outcomes linked specifically to the SCI (Bonanno et al., 2012; van Leeuwen, Kraaijeveld, Lindeman, & Post, 2012; Dean & Kennedy, 2009). This study now clearly demonstrates that the way an injury is appraised also has important consequences for individuals with regards to their pain. When combined, pain catastrophizing and injury appraisal mediated the effects of almost all other variables on all of the pain outcomes, suggesting that these two factors need particular attention during rehabilitation and in pain management programmes.

12.3 **Key Social Outcomes**

Much research in the able-bodied literature has indicated that solicitousness from a significant other has detrimental consequences to the person in pain. For example, it can lead to increased functional limitations and reduced physical activity (Hemphill, Martire, Polenick, & Parris Stephens, 2016; Raichle, Romano, & Jensen, 2011). In the SCI population, however, it has been suggested that solicitous responses may be beneficial (Widerström-Noga et al., 2007; Stroud et al., 2006), improving activity engagement and reducing pain-related distress. The results of this study provide some support for this. Fewer solicitous responses were received by the out-patient group than by the in-patient group and this was found alongside less determined

resilience, greater negative injury appraisal and lower pain acceptance. Whilst cause cannot be established here, given the previous literature, it does imply that fewer solicitous responses from a significant other might be associated with poorer outcomes in this population. This is supported by the mediation analysis, which found that solicitousness had a direct positive effect on support. This indicates that people with SCI perceived that they had greater support when a significant other responded to their pain in a solicitous manner. This is important because people with SCI have said that support from family and friends is indispensable in their adaptation to the injury (Duggan, Wilson, DiPonio, Trumpower, & Meade, 2016). However, Newton-John (2013) has also suggested that people in a caring role might experience carer burnout, where their ability to provide emotional support becomes depleted. This might explain the difference in solicitous responses perceived between the in-patient and out-patient groups, and indicates that carers may need support in their role if people with SCI are to adapt well to their injury.

The literature regarding distracting responses has been mixed in the spinal cord injured population, with some reporting the benefits of distraction (Widerström-Noga et al., 2007) and others reporting negative outcomes (Taylor et al., 2012). The results of the regression analysis in this study found that a distracting response predicted greater interference from pain. However, determined resilience (as an appraisal of injury) mediated the effects of distracting responses on pain-related distress, life control and engagement in activities. If people received more distracting responses, they demonstrated greater determined resilience concerning their injury, which resulted in reduced pain-related distress, higher sense of control and engagement in more activities. This suggests that determined resilience makes the difference between whether distracting responses result in more negative or in more positive pain outcomes. Appraisal of injury also proved to be an important mediator between negative responses and pain outcomes, with both negative appraisals and determined resilience individually and in combination being influential. This provides additional evidence for the wide-ranging effects of injury appraisal both from a psychological perspective but also where the responses of others are concerned.

However, the results of this study raise the question of how people perceive the responses they get from other people to their expression of pain. For example, it would be useful to know whether distracting and solicitous responses are seen as helpful or as interfering. This is an important question because how the intention behind the response is appraised by the person in pain, has a greater influence on the consequences of pain than the actual response given (Lewandowski, Morris, Draucker, & Risko, 2007). Therefore, the appraisal of another person's response can impact on pain outcomes which can then affect adaptation to injury. Over all, the distracting and solicitous responses of significant others did not have as great an impact on pain outcomes as expected. It is possible that they have a more influential role as mediators, rather than as predictors.

12.4 Clinical Implications, Study Limitations, and Future Directions

12.4.1 Clinical Implications

It is of concern that people with SCI and pain experience a worsening of their biopsychosocial outcomes after leaving hospital and their rehabilitation programmes. Clinically, these results suggest that there is a need to identify and red-flag post-hospital risks for people with SCI and pain. These risks include more negative appraisals of injury, increased depression and mental defeat, lower pain acceptance, less social support and more catastrophic thinking. Regular out-patient appointments, which monitor the psychosocial factors, as well as the physical difficulties being experienced, could mitigate against this and enable prompt diagnosis and treatment. Out-patient rehabilitation programmes have been found to be effective in aiding functional recovery and complementing in-patient programmes (Derakhshanrad, Vosoughi, Yekaninejad, Moshayedi, & Saberi, 2015).

Additionally, the results of this study suggest that these appointments require less emphasis on the biomedical model, and a greater involvement of the clinical psychology team. This supports previous research which found that,

for people with SCI, psychological treatment strategies are more successful in pain management than relying solely on pharmacological treatments (Heutink, Post, Wollaars, & van Asbeck, 2011). Similarly, it is important for clinicians to recognise that pain intensity is only one facet of pain management, and that the other affective and functional outcomes of pain also need to be attended to. Indeed, Borsbo, Peolsson and Gerdle (2009) found that it was the psychological factors rather than pain intensity or duration that had the greatest negative impact on quality of life and pain-related disability, whilst Widerström-Noga et al. (2007) found that even with high pain intensity, people had better outcomes if they also had good social support. This indicates that clinicians need to operate from a biopsychosocial perspective when working with people with SCI and pain.

Because people often have to travel long distances to attend out-patient clinics for SCI (Cox, Amsters, & Pershouse, 2001), more community-based resources need to be made available to people once they leave hospital. However, it has been found that health professionals in the community often do not have the necessary skills and knowledge about SCI (Cox, Amsters, & Pershouse, 2001; Neri & Kroll, 2003). Therefore training needs to be provided for community health professionals so that they can identify indications of psychosocial problems early on and sign-post people for additional support. This is particularly important given that the further people have to travel, the less likely they are to utilise health resources (LaVela, Smith, Weaver, & Miskevics, 2004). An alternative might be to explore the use of online health resources, telephone advice, and telehealth, which has been receiving more attention in the spinal cord injured population. For example, Cox et al. (2001) found that 79% of their participants with SCI would value the opportunity of accessing telephone health lines for advice about their health. Similarly, the use of telehealth technologies have been found useful for helping people with SCI remain in the community and avoid re-hospitalisation (Woo, Guihan, Frick, Gill, & Ho, 2011).

Pain management programmes need to acknowledge that mindfulness and pain acceptance may work differently for people with SCI, and that aspects of

mindfulness such as staying in the present moment may cause greater distress (Dorado, et al., 2018). Focusing on activities that assist the individual in working towards achieving their rehabilitation goals, a focus on the future, might be more beneficial. Also, it is important to acknowledge in pain management programmes, that seeking to solve the problem of pain could be an important step in being able to eventually live well in the presence of pain (Henwood et al., 2012). Additionally, interventions that aim to reduce pain catastrophizing and improve the way the injury is appraised will help as these are important mediators between acceptance and pain outcomes.

Two psychological variables that emerged as being particularly influential for people with SCI and pain were pain catastrophizing and appraisal of injury. These factors were identified as being important as predictors but were particularly strong as mediators between the other biopsychosocial variables and pain outcomes. This suggests that greater attention needs to be given by clinicians to those people displaying high catastrophic thinking and/or who appraise their injury negatively, demonstrating lower determined resilience. Regular screening for both of these could be incorporated within in-patient rehabilitation programmes and as a standard assessment at each out-patient appointment. This would allow for relevant psychological interventions to be activated in a timely manner, which could reduce the negative effects on adjustment and pain outcomes. This is important as both negative appraisal of injury (Bonanno et al., 2012; Dean & Kennedy, 2009) and higher catastrophic thinking (Kim, Williams, Hassett, & Kratz, 2019) have been associated with poorer adjustment and pain outcomes. As well as screening for indications of pain catastrophizing and negative injury appraisal, interventions that aim to develop resilience and reduce catastrophic negativity regarding the injury should become a standard part of rehabilitation programmes. This study supports previous research (e.g. Kennedy et al., 2010; Craig et al., 2015) in suggesting that determined resilience and catastrophic negativity mediate the effects on different consequences of pain. Proactively focusing on developing the former and reducing the latter could therefore, impact positively on a wide range of pain outcomes.

12.4.2 Study Limitations

This study has provided additional information to the current literature that can inform clinicians in treating people who experience pain alongside of their SCI. However certain limitations are apparent, which means that some of the results should be treated with caution.

The in-patient longitudinal study had a high drop-out rate of 51%, which lead to only 29 people being included in the second and third time point data collections. Because of this the ANOVAs used in the longitudinal analysis, and the t-tests comparing in-patient time 3 and out-patient groups were underpowered. This may have increased the risk of a Type 1 error, where a false positive is obtained, or a Type 11 error, where the null hypothesis is incorrectly supported; a false negative. The data collection for the in-patient group took place over a two-year period by a single researcher. Each data collection took between 45 and 60 minutes so the practical demands were high. Continuing the data collection beyond two years was not feasible and so it was not possible to obtain a larger sample. At the second and third data collection time points every participant was phoned or emailed to ask if they were happy to continue with the study. Once consent had been obtained, individuals were sent two reminders (by phone or email) if they failed to return their questionnaires and saliva samples. It was decided that more than two reminders could be construed as exerting undue pressure. In short, sufficient numbers were recruited initially and every effort was made to minimise the drop-out rate. It has been noted previously that because of the relatively low incidence rate of SCI and the complexities associated with the condition, keeping participants engaged in longitudinal studies is particularly challenging (Craig et al., 2015). The attrition rate in this study is comparable to that found in other studies. Gustavson, von Soest, Karevold, and Røysamb (2012) reported that dropout rates between 30% and 70% are common in health research. More importantly, they conclude that even when attrition rates are high, longitudinal studies looking at protective / risk factors for health outcomes are valuable.

All individuals who had reported experiencing pain were invited to take part in the study. However, it is not known whether those who declined to participate had any characteristics that were significantly different to those who engaged with the research. Therefore, it is not known whether this represents a biased sample. For example, it is possible that people who chose not to take part may have had greater psychological difficulties, given that individuals who were known to have severe mental health problems were not approached. Additionally, people with psychological disorders who were invited may have been less likely to volunteer. This would support Craig et al. (2015) who suggested that the rate of psychological disorders in their study could have been underestimated for these reasons. However, participants provided a wide range of responses on each of the questionnaires, and had a range of demographic characteristics, apart from ethnicity. This does not indicate that a narrow sample was obtained.

Data on the use of medication and rehabilitation treatments was not collected and it is feasible that these could have had an impact on the factors included in this study. For example, some of the participants are likely to have been taking anti-depressants. This type of medication is known to also have anti-nociceptive properties so that people with depression may have had reduced pain because of it. Similarly, many would have been on pain medication, with a similar outcome. However, the focus of this study was the pain they were actually experiencing, its outcomes and predictors. This data was collected, therefore, whether the pain was masked or not was of less importance.

The study relied on self-report measures which are open to social desirability bias, and which may have increased the strength of associations artificially. This is particularly a problem in SCI where test scores may be inflated by some of the other symptoms being experienced, such as sleep loss (Craig et al., 2015). Best practice recommends that diagnostic psychiatric interviews are used alongside psychometric measures when measuring variables such as depression and anxiety (Graves & Bombardier, 2008). This was not possible for this study as the researcher was not qualified in this area, so the risks were minimised as far as possible by using validated measures, some of which had

been designed specifically for people with SCI.

For the multiple regression analyses, the affective, sensory and functional subscales of the MPI-SCI section A were used as the two other subscales of 'support' and 'life control' were of less interest in this part of the analysis. However, using only these subscales may have reduced the psychometric properties of the questionnaire. Therefore the validity and reliability of this measure should be considered tentatively.

Compliance with the cortisol protocol cannot be assured with regards to people in the out-patient group. They were sent the packs by post, with clear instructions and then provided the sample and returned it. It is not possible to be certain that they provided samples at the required time of day or that they adhered to the protocol regarding avoidance of food, drink, exercise, and smoking in the hour prior to taking the saliva swab. However, all possible controls were used and people were asked to confirm that they had abided by the instructions and state the precise time that they took the sample. There were no significant differences between the in-patient and out-patient groups which suggests that in the main individuals did comply with the directions.

An additional limitation with regards to the cortisol collection was that as it was only provided on one occasion, and at a particular time of day, it might have resulted in less precise estimates than if it had been collected on a number of occasions in a single day. Additionally, because individual differences exist in the diurnal cortisol pattern, and it was not possible to establish benchmark measures for individuals, classifying cortisol as either high or low is problematic. Therefore, the results relating to cortisol and its relationship with other variables in this study need to be treated with caution. An alternative way of analysing cortisol is through hair samples, which can show changes in concentration levels over time, depending on the length of hair taken. If cortisol had been analysed through hair samples it would have provided a look back in time, allowing an indication of pre-injury cortisol levels and potentially pre-injury distress, which could be useful for determining post-injury recovery trajectories (Walton, MacDermid, Russell, Koren, & Van Uum, 2013).

However, hair samples are not as acceptable to participants and need at least 3cm (1cm per month) to get a reasonable look back in time (Walton et al, 2013). This potentially could have resulted in a biased sample of younger and/or female participants who may have longer hair. It was considered that saliva sampling would be much more acceptable to this population. Additionally, the analysis of diurnal patterns was not the aim of this study, which was to compare cortisol concentration to other psychosocial variables. The single sample enabled this, although because of the lack of benchmark cortisol measures for each individual the results should be treated with caution.

Much of the existing literature concerning the variables included in this study comes from Europe, North America and Australia, with a lack of prevalence data available for the UK. It is possible that treatment within the National Health Service and the experiences of people with SCI in the UK are very different to those in other countries. Therefore, it is not possible to draw firm conclusions or generalize the existing evidence base to the SCI population in the UK. Additionally, this study only included participants from one hospital, and their treatment may be different to that in hospitals in other parts of the country. Generalising the results from this study to the wider UK SCI population should be done with caution. A greater emphasis on international and multi-centre studies is required to bridge this gap.

12.4.3 Future Directions

The results of this study found a clear relationship between cortisol concentration and pain outcomes when mediated by catastrophic thinking. As little research has focused on cortisol in the spinal cord injured population, further studies are needed to verify these results. Additionally, the reasons for the decline in cortisol over time requires clarifying to determine whether it reflects hypocortisolism or a return to premorbid levels. The use of hair samples is one way of doing this as they would provide information about cortisol concentration prior to the injury (Walton, MacDermid, Russell, Koren & Van Uum, 2013). This could then be compared to samples taken later during

rehabilitation and post discharge. It is important to do this because of the particular risks associated with hypocortisolism for people with SCI.

Appraisal of injury emerged as an important mediator between psychosocial factors and pain outcomes, demonstrating its influence where pain is concerned. As this is one area that appears to become more negative over time, and its impact is high, interventions that seek to increase determined resilience and reduce catastrophic negativity need to be designed and trialled as part of the standard rehabilitation programme. Kennedy, Duff, Evans and Beedie (2003) found that training in effective coping, an indication of resilience, reduced symptoms of anxiety and depression. If successful, therefore, interventions aimed at improving injury appraisal could lead to better pain and adaptation outcomes.

The results of this study also suggested that there may be a reciprocal relationship between injury appraisal and other psychosocial variables. Given its mediating power, it is important to understand whether such reciprocal relationships exist, as they might reflect a spiralling downward following discharge, partly explaining the worsening of certain symptoms over time that was highlighted by this study. Future longitudinal research needs to explore whether this is an associated factor, and what else might contribute to the decline experienced by people once they have left hospital. Additionally, it is possible that, rather than symptoms worsening over time, they are simply being masked whilst in hospital, and remaining poor following discharge. Research to explore this would prove useful as it may highlight additional rehabilitation requirements.

Although this study has contributed to the knowledge and understanding of pain in SCI, further research could shed additional light on which aspects of the pain experience are different for this group in comparison to the able-bodied pain population. It has emerged for example, that pain acceptance might operate differently for people with pain and SCI than for those with pain but without an injury. Such a study could also compare people with pain who are coping well and people in pain who are experiencing greater difficulties, to

provide greater clarity on which factors are protective and which represent a risk.

Lastly, further research is necessary to clarify the impact of a significant other's response to the individual in pain. This study did not find that significant others' responses had a high mediated effect on pain outcomes. It is possible therefore, that the way a significant other responds to someone in pain is itself a mediator between other factors and the consequences of pain. Future research could explore whether such responses have a mediating role, and the effects of which predictors are mediated on which outcomes.

Solicitousness has been found to be beneficial for people with SCI (Widerström-Noga, Felix, Cruz-Almeida, & Turk, 2007) and this was supported in this study. Therefore, an exploration as to why out-patients received fewer solicitous responses than in-patients could inform the type of support that carers require in order to support someone with a SCI in the longer term. Alongside of this it would also be useful to examine whether this reduction in solicitousness is a result of caregiver burnout as described by Ybema, Kuijer, Hagedoorn, and Buunk (2002) and Newton-John (2013).

An additional question raised in this study pertained to how the responses of others are more generally perceived by someone in pain. The perceived response has been found to be more important than the actual response where pain is concerned (Lewandowski, Morris, Draucker, & Risko, 2007) so seeking greater clarity about this is important. Of particular interest is how solicitous and distracting responses are perceived by people with SCI, and in comparison, how those responses are intended by the giver of them. Qualitative research could shed further light on this through the use of semi-structured interviews with the individual in pain and the significant other person. It might be that a greater emphasis needs to be placed on educating carers of people with SCI about the significance of their behaviour and the impact it may have. This could happen as part of the rehabilitation process, whilst the individual is still in hospital. Additionally, once the individual leaves hospital, on-going carer support initiatives could be trialled to assess how

helpful they might be in providing longer term practical and emotional advice and encouragement.

12.4.4 Conclusion

The primary aim of this thesis was to explore the way biopsychosocial factors interact to impact on the pain experience in people with a SCI. In doing this, it was intended that the knowledge base in this area would be expanded, providing evidence to inform the treatment of pain during and after primary rehabilitation. To do this variables from all three elements of the biopsychosocial model were examined, and the Foundational Principles in rehabilitation psychology were used to guide the design and implementation of the study.

The inclusion of biological, psychological and social variables has highlighted important interactions between them. Two psychological variables emerged to be particularly influential where the consequences of pain were concerned: appraisal of injury and pain catastrophizing. These factors mediated the effects of each of the biopsychosocial predictors on all the pain outcomes. Pain catastrophizing was particularly influential in mediating the effects of cortisol and injury appraisal was a strong mediator of the responses of significant others. Both were influential mediators between the other psychological factors and pain outcomes. Whilst both injury appraisal and catastrophic thinking mediated the effects on the functional consequences of pain, they affected the sensory and affective pain outcomes differently, with pain catastrophizing being more influential on the former, and injury appraisal having a greater effect on the latter. Therefore, in combination, the impact of these two variables is widespread. Given that research has not explored the association between appraisal of SCI and pain before, this interaction is of particular importance where the treatment of pain is concerned. In addition, this study highlighted that some people do poorly once they leave hospital, therefore including a focus on injury appraisal and pain catastrophizing in the treatment of pain could have far reaching and positive implications with regards to pain management and its consequences on adjustment to injury.

This study has clearly demonstrated that a focus on any one of the biopsychosocial elements in isolation risks missing the effects they each have on pain when combined with the others. Pain management programmes, therefore, need to be provided alongside of pain medication and be firmly grounded in the biopsychosocial model. This involves interventions with SCI patients to improve appraisal of injury, reduce catastrophic thinking and build resilience, and interventions with primary carers to provide support, develop their knowledge base and reduce the risk of caregiver burnout. These types of interventions need to be provided during rehabilitation but research also needs to explore how they can be made available to, and accessed by people once they have transitioned back into the community. Providing programmes of this nature could reduce the reliance on pain medication, and the longer term and on-going need for referrals to healthcare professionals. Most importantly, such programmes could improve adjustment to injury, quality of life, and enable people to live well with SCI and pain.

13 Appendix 1 - Glossary of Biological Terms

Adrenal cortex	Outer part of adrenal gland
Adrenaline	Stress hormone produced in the adrenal gland
Adrenocorticotropic hormone (ACTH)	Hormone secreted by pituitary gland which stimulates the adrenal cortex
Allostatic load	Wear and tear on the body
Amygdala	Almond-shaped grey matter associa with emotion and fear
Anterior cingulate cortex	Frontal part of the cingulate cortex associated with autonomic function
Anterior lateral system	Bundle of fibres containing the spino – reticular, thalamic and mesencephalic tracts
Arginine vasopressin	Hormone secreted by cells of the hypothalamus
Autonomic nervous system	Nervous system responsible for cont of bodily functions
Basal forebrain	Located in the forebrain, produces acetylcholine, associated with wakefulness and REM sleep
Basolateral amygdala	Largest cluster of neurons in the amygdala, receives input from sensory cortices.
Bed nucleus of the stria terminalis	Regulates HPA activity in response to acute stress
Brainstem	Consists of the medulla, pons and midbrain. Continues to form spinal cord.
Brodmann's area 8	Part of the frontal cortex
Central nucleus of the amygdala	Receives and processes pain information

Corticosteroid hormone	A class of steroid hormone
Corticotropin- releasing factor (CRF)	A peptide hormone associated with stress response
CRF type 1 receptors	Receptor cells in the anterior pituitary gland.
Cyclic adenosine monophosphate pathway	A second messenger used to transduce signals intracellularly
Diacylglycerol	A secondary messenger that can relay and amplify signals.
Diffuse noxious inhibitory control	A pain modulatory pathway
Dopamine	A neurotransmitter associated with reward-motivated behaviour
Dorsal Horn	A column of the spinal cord that receives sensory information from the body.
Dorsal reticular nucleus	Part of the supraspinal pain control system.
Dorsal thalamus	Posterior part of the thalamus.
Dorso-medial thalamus	Large nucleus in the thalamus associated with memory and executive tasks.
Dorsolateral pontine tegmentum	Part of the pons in the brainstem, associated with for example, sensory and motor functions, sleep stages and respiratory control.
Dorsolateral prefrontal cortex	Part of the frontal lobe associated with executive functions, e.g., working memory
Glucocorticoid	A class of corticosteroids and part of the feedback process in the immune system.
Hippocampus	Part of the limbic system associated learning, memory and emotion.

Hypercortisolism	Excess cortisol produced.
Hypocortisolism	Adrenal glands do not produce enough cortisol.
Hypothalamic-Pituitary- Adrenal axis	Stress response system.
Hypothalamo-pituitary portal circulation	A system of blood vessels connecting the hypothalamus and pituitary gland.
Hypothalamus	Located near the pituitary gland and associated with body temperature regulation and the stress response.
Inferior thalamic nucleus	One of the nuclear groups of the thalamus.
Inositol triphosphate	A secondary messenger that can relay and amplify signals.
Insula	Located in the lateral sulcus, which separates the temporal lobe from the frontal and parietal lobes. Believed to be involved in self-awareness and perception.
Interleukin - 6	A pro-inflammatory cytokine that mediates fever and the acute phase reaction in response to inflammation
Lateral amygdala	Area of the amygdala associated with fear conditioning
Limbic system	A collection of structures associated emotion, learning, memory and motivation.
Locus Coeruleus	A nucleus in the pons associated with the physiological response to stress.
Medulla	Located in the brainstem and involved with autonomic functions.
Melanocortin type 2 receptor	An ACTH receptor.

Microglial cells	Cells of the central nervous system, important for maintaining its health.
Noradrenaline	A catecholamine functioning as a neurotransmitter & hormone
Nucleus raphe magnus	Located in the brainstem, they inhibit pain and alter serotonin levels for sleep and wakefulness.
Paraventricular nuclei of the hypothalamus	A group of neurons involved in a range of autonomic functions including the control of stress.
Parietal lobe	Located at the top of the brain and receives sensory inputs, e.g. pain, Touch, temperature. Also involved in proprioception.
Parvocellular neurosecretory cells	Small neurons in the hypothalamus associated with the HPA axis process.
Periaqueductal grey	Primary area for descending pain modulation.
Pituitary gland	Located behind the nose, it controls thyroid, adrenal galnds, ovaries and testicles. Part if the HPA axis.
Prefrontal cortex	Part of the brain located at the front of the frontal lobe
Primary sensory cortex	Located in the parietal lobe and responsible for sensory information.
Proinflammatory cytokines	Signaling molecules that mediate inflammation
Reticular formation	Located in the brainstem and associated with pain modulation.
Reticulospinal fibres	Descending pathway from the reticular formation to the spinal cord.
Rostral ventromedial medulla	Part of the medulla, and sends

	descending inhibitory or excitatory messages to the dorsal horn in the spinal cord.
Serotonin	A monoamine neurotransmitter with wide range of biological functions.
Spinomesencephalic tract Spinoreticular tract Spinothalamic tract	Pathways transmitting pain messages from the dorsal horn to various parts of the brain for the complete pain experience.
Substantia gelatinosa	Cells of the dorsal horn that receive input from pain and thermoreceptors
Temporomandibular Disorder	A condition causing pain in the jaw joint and associated muscles.
Thalamus	Relays sensory and motor signals to the cerebral cortex.
Tumor necrosis factor	A protein that causes inflammation to help fight infection etc.
Vasopressin V1B receptor	A receptor for vasopressin and involved in homeostasis.
Ventral posterior lateral thalamic nucleus	Receives information from the spinothalamic tracts and projects to somatosensory cortex.
Ventrolateral prefrontal cortex	Part of prefrontal cortex involved in control and inhibition.
Ventromedial prefrontal cortex	Part of the prefrontal cortex involved emotion regulation

14 Appendix 2 – Frequency Counts For Demographic Data

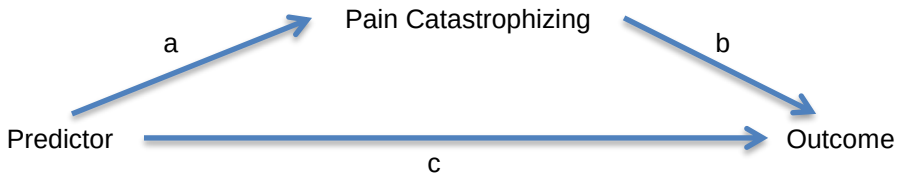
Demographic Variable	Time 1 Only			Time 1 & Time 2			Time 1 & Time 3			All Time Points			Total Obs
	Ex	Obs	%	Ex	Obs	%	Ex	Obs	%	Ex	Obs	%	
Injury Type													
- CT	2.0	2	50	0.5	1	25	0.4	0	0	1.1	1	25	4
- IT	10.2	13	65	2.4	1	5	2.0	2	10	5.4	4	20	20
- CP	2.0	1	25	0.5	2	50	0.4	0	0	1.1	1	25	4
- IP	15.8	14	45	3.7	3	10	3.2	4	13	8.4	10	32	31
Total Obs		30			7			6			16		59
Injury Level													
- Cervical	15.8	17	55	3.7	4	13	3.2	2	6	8.4	8	26	31
- Thoracic	10.2	9	45	2.4	2	10	2.0	3	15	5.4	6	30	20
- Lumbar	4.1	4	50	0.9	1	12.5	0.8	1	12.5	2.2	2	25	8
Total Obs		30			7			6			16		59
Injury Cause													
- RTA	5.7	5	46	1.3	2	18	1.1	1	9	2.9	3	27	11
- Fall	7.8	9	60	1.8	0	0	1.5	3	20	4.0	3	20	15
- Sport	4.1	3	37.5	0.9	1	12.5	0.8	1	12.5	2.1	3	37.5	8
- Non-trauma	4.7	3	33	1.1	3	33	0.9	0	0	2.4	3	33	9
- Other	8.3	10	63	1.9	1	6	1.6	1	6	4.3	4	25	16
- Not stated	0.5	1	100	0.1	0	0	0.1	0	0	0.3	0	0	1
Total Obs		31			7			6			16		60
Relationship Status													
- Single	9.3	14	78	2.1	2	11	1.8	0	0	4.8	2	11	18
- Cohabiting	1.6	1	33.3	0.4	0	0	0.3	1	33.3	0.8	1	33.3	3
- Married	14.0	10	37	3.2	3	11	2.7	3	11	7.2	11	41	27
- Divorced	3.1	1	17	0.7	1	17	0.6	2	33	1.6	2	33	6
- Widowed	2.6	5	100	0.6	0	0	0.5	0	0	1.3	0	0	5
- Separated	0.5	0	0	0.1	1	100	0.1	0	0	0.3	0	0	1
Total Obs		31			7			6			16		60

Demographic Variable	Time 1 Only			Time 1 & Time 2			Time 1 & Time 3			All Time Points			Total Obs
	Ex	Obs	%	Ex	Obs	%	Ex	Obs	%	Ex	Obs	%	
Education													
- None	2.6	4	80	0.6	0	0	0.5	0	0	1.3	1	20	5
- GCSE	8.8	7	41	2.0	3	18	1.7	2	12	4.5	5	29	17
- A' Level	9.8	13	69	2.2	1	5	1.9	0	0	5.1	5	26	19
- Degree	5.7	4	37	1.3	1	9	1.1	3	27	2.9	3	27	11
- Postgraduate	2.1	1	25	0.5	1	25	0.4	0	0	1.1	2	50	4
- Other	2.1	2	50	0.5	1	25	0.4	1	25	1.1	0	0	4
Total Obs		31			7			6			16		60

Note: Frequency counts for demographic data of participants participating at time 1 only, time 1 and time 2 only, time 1 and time 3 only or all time points in the longitudinal in-patient study.CT=Complete Tetraplegia; IT=Incomplete Tetraplegia; CP=Complete Paraplegia; IP=Incomplete Paraplegia. Ex = Expected count; Obs = Observed count; % = Percentage within demographic variable

15 Appendix 3 - Mediation Analysis Statistical Results

Mediator: Pain Catastrophizing



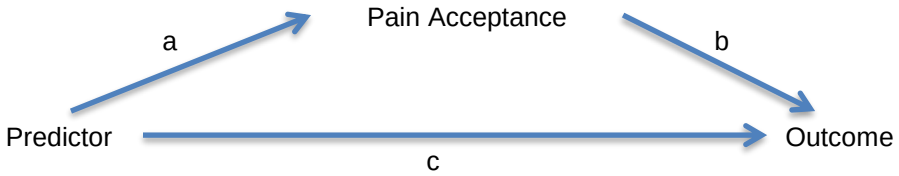
Predictor	Outcome	a	b	c	Direct	Indirect
Cortisol	Pain Intensity Life Interference Distress Life Control MPICb	*b* = 7.24, *p* = .190	***b* = 0.06, *p* = .002** ***b* = 0.47, *p* <.001** ***b* = 0.11, *p* = .005** ***b* = -0.13, *p* <.001** ***b* = 0.97, *p* <.001**	*b* = -0.94, *p* = .253 *b* = 1.72, *p* = .712 *b* = 0.90, *p* = .595 *b* = -0.26, *p* = .874 *b* = -4.37, *p* = .721	*b* = -1.36, *p* = .081 *b* = -1.65, *p* = .680 *b* = 0.11, *p* = .947 *b* = 0.71, *p* = .637 *b* = -11.39, *p* = .313	***b* = 0.42, CI [0.13, 4.24]** ***b* = 3.37, CI [1.43, 39.79]** ***b* = 0.79, CI [0.20, 10.98]** ***b* = -.096, CI [-12.82, -0.33]** ***b* = 7.03, CI [2.06, 98.85]**
Depression	Pain Intensity Life Interference Distress Life Control MPICb	***b* = 1.91, *p* <.001** *b* = 7.24, *p* = .190	***b* = 0.07, *p* = .008** ***b* = 0.27, *p* = .032** *b* = 0.04, *p* = .370 *b* = -0.08, *p* = .064 ***b* = 0.94, *p* = .032**	*b* = 0.09, *p* = .172 ***b* = 1.83, *p* <.001** ***b* = 0.70, *p* <.001** ***b* = -0.49, *p* <.001** *b* = 1.84, *p* = .075	*b* = -0.05, *p* = .534 ***b* = 1.32, *p* <.001** ***b* = 0.63, *p* <.001** ***b* = -0.32, *p* = .024** *b* = -0.09, *p* = .942	***b* = 0.14, CI [0.05, 0.23]** *b* = 0.51, CI [-0.07, 0.97] *b* = 0.07, CI [-0.13, 0.25] *b* = -0.17, CI [-0.35, 0.001] ***b* = 1.80, CI [.001, 3.26]**
ADAPSS Negativity	Pain Intensity Life Interference Distress Life Control MPICa	***b* = 0.69, *p* <.001**	***b* = 0.06, *p* = .007** *b* = 0.18, *p* = .103 *b* = 0.06, *p* = .191 *b* = -0.06, *p* = .152 *b* = -0.04, *p* = .854	*b* = 0.02, *p* = .159 ***b* = 0.50, *p* <.001** ***b* = 0.14, *p* <.001** ***b* = -0.15, *p* <.001** ***b* = -0.30, *p* = .041**	*b* = -0.02, *p* = .376 ***b* = 0.38, *p* <.001** ***b* = 0.10, *p* = .024** ***b* = -0.12, *p* = .008** *b* = -0.32, *p* = .134	***b* = 0.04. CI [0.01, 0.08]** *b* = 0.12, CI [-0.04, 0.30] *b* = 0.04, CI [-0.02, 0.11] *b* = -0.04, CI [-0.12, 0.01] *b* = 0.03, CI [-0.31, 0.27]

	MPICb		*b* = 0.25, *p* = .490	***b* = 0.91, *p* <.001**	***b* = 0.75, *p* = .044**	*b* = 0.17, CI [-0.45, 0.71]
ADAPSS Resilience	Pain Intensity Life Interference Distress Support Life control MPICa MPICb	***b* = -0.53, *p* <.001** ***b* = -0.53, *p* <.001**	***b* = 0.06, *p* = .001** ***b* = 0.42, *p* <.001** ***b* = 0.08, *p* = .013** *b* = 0.05, *p* = .188 ***b* = -0.09, *p* = .004** *b* = -0.09, *p* = .586 ***b* = 0.82, *p* = .006**	*b* = -0.00, *p* = .988 ***b* = -0.32, *p* = .014** ***b* = -0.20, *p* <.001** ***b* = 0.13, *p* = .014** ***b* = 0.21, *p* <.001** ***b* = 0.61, *p* = .002** *b* = -0.25, *p* = .490	*b* = 0.03, *p* = .195 *b* = -0.09, *p* = .446 ***b* = -0.15, *p* <.001** ***b* = 0.15, *p* = .006** ***b* = 0.16, *p* <.001** ***b* = 0.57, *p* = .007** *b* = 0.19, *p* = .627	***b* = -0.03 CI [-0.07, -0.01]** ***b* = -0.22, CI [-0.41, -0.09]** ***b* = -0.05, CI [-0.12, -0.01]** *b* = -0.03, CI [-0.10, 0.02] ***b* = 0.05, CI [0.01, 0.10]** *b* = 0.05, CI [-0.12, 0.27] ***b* = -0.44, CI [-0.94, -0.10]**
Acceptance	Pain Intensity Life Interference Distress Support Life Control MPCIb	***b* = -0.15, *p* = .015**	***b* = 0.06, *p* <.001** ***b* = 0.45, *p* <.001** ***b* = 0.13, *p* <.001** *b* = 0.04, *p* = .276 ***b* = -0.14, *p* <.001** ***b* = 0.82, *p* = .004**	*b* = 0.01, *p* = .308 *b* = -0.06, *p* = .262 *b* = -0.02, *p* = .321 ***b* = 0.06, *p* = .003** *b* = 0.02, *p* = .298 *b* = -0.03, *p* = .858	***b* = 0.02, *p* = .045** *b* = 0.01, *p* = .851 *b* = 0.00, *p* = .984 ***b* = 0.07, *p* = .002** *b* = -0.001, *p* = .935 *b* = 0.10, *p* = .508	***b* = -0.01, CI [-0.02, -0.00]** ***b* = -0.07, CI [-0.14, -0.01]** ***b* = -0.02 CI [-0.05, -0.00]** *b* = -0.01, CI [-0.02, 0.01] ***b* = 0.02, CI [0.001, 0.05]** ***b* = -0.13, CI [-0.31, -0.01]**
Anxiety	Pain Intensity Life Interference Distress Life Control MPICb	***b* = 1.04, *p* <.001**	*b* = 0.03, *p* = .545 ***b* = 0.34, *p* <.001** ***b* = 0.07, *p* = .029** ***b* = -0.09, *p* = .003** ***b* = 0.64, *p* = .026**	*b* = 0.03, *p* = .545 ***b* = 1.12, *p* <.001** ***b* = 0.51, *p* <.001** ***b* = -0.40, *p* <.001** ***b* = 1.63, *p* = .025**	*b* = -0.03, *p* = .562 ***b* = 0.77, *p* = .001** ***b* = 0.44, *p* <.001** ***b* = -0.31, *p* <.001** *b* = 0.96, *p* = .206	***b* = 0.06, CI [0.01, 0.13]** ***b* = 0.35, CI [0.12, 0.62]** ***b* = 0.07, CI [0.003, 0.16]** ***b* = -0.09 CI [-0.18, -0.03]** ***b* = 0.67, CI [0.01, 1.63]**
Negative Response	Life Interference Distress	*b* = 0.40, *p* = .096	***b* = 0.41, *p* <.001** ***b* = 0.12, *p* <.001**	***b* = 0.58, *p* = .004** ***b* = 0.20, *p* = .006**	***b* = 0.41, *p* = .019** ***b* = 0.15, *p* = .026**	*b* = 0.17, CI [-0.01, 0.40] *b* = 0.05, CI [-0.002, 0.12]
Distracting Response	Support	*b* = 0.26, *p* = .308	*b* = -0.02, *p* = .585	***b* = 0.46, *p* <.001**	***b* = 0.47, *p* <.001**	*b* = -0.01, CI [-0.04, 0.03]
Solicitous Response	Support	*b* = 0.19, *p* = .347	*b* = -0.01, *p* = .712	***b* = 0.32, *p* <.001**	***b* = 0.33, *p* <.001**	*b* = -0.002, CI [-0.03, 0.02]
Mental Defeat	Pain Intensity Life Interference Distress	***b* = 0.36, *p* <.001**	*b* = 0.03, *p* = .255 ***b* = 0.30, *p* = .018** *b* = 0.06, *p* = .226	***b* = 0.02, *p* = .003** ***b* = 0.20, *p* <.001** ***b* = 0.07, *p* <.001**	*b* = 0.01, *p* = .270 *b* = 0.09, *p* = .125 *b* = 0.04, *p* = .060	*b* = 0.01, CI [-0.01, 0.03] ***b* = 0.11, CI [0.01, 0.19]** *b* = 0.02, CI [-0.02, 0.06]

	Life Control MPICb		*b* = -0.08, *p* = .095 ***b* = 0.98, *p* = .017**	***b* = -0.07, *p* <.001** *b* = 0.23, *p* = .082	*b* = -0.04, *p* = .090 *b* = -0.12, *p* = .519	*b* = -0.03, CI [-0.06, 0.01] ***b* = 0.35, CI [0.06, 0.64]**
Stress	Pain Intensity Life Interference Distress Life Control MPICb	***b* = 0.87, *p* <.001**	***b* = 0.06, *p* = .002** ***b* = 0.40, *p* <.001** *b* = 0.05, *p* = .119 ***b* = -0.08, *p* = .019** ***b* = 0.95, *p* = .002**	*b* = 0.01, *p* = .675 ***b* = 0.53, *p* = .001** ***b* = 0.31, *p* <.001** ***b* = -0.27, *p* <.001** *b* = 0.25, *p* = .596	*b* = -0.04, *p* = .214 *b* = 0.18, *p* = .280 ***b* = 0.27, *p* <.001** ***b* = -0.20, *p* = .001** *b* = -0.57, *p* = .276	***b* = 0.05, CI [0.02, 0.10]** ***b* = 0.35, CI [0.16, 0.58]** *b* = 0.05, CI [-0.02, 0.12] ***b* = -0.07, CI [-0.14, -0.01]** ***b* = 0.82, CI [0.29, 1.44]**

Note: The confidence intervals for the indirect effect is a BCa bootstrapped CI based on 5000 samples. Significant results are shown in bold print.

Mediator: Pain Acceptance



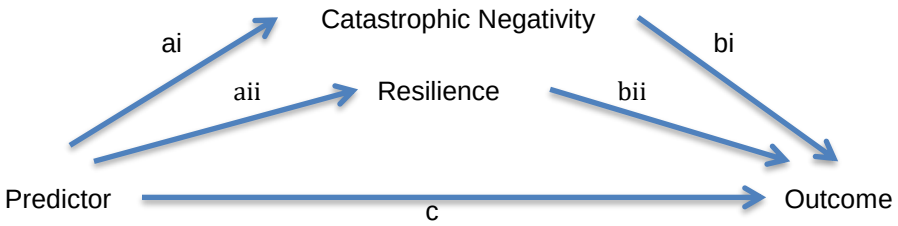
Predictor	Outcome	a	b	c	Direct	Indirect
Depression	Life Interference Distress Life Control MPICb	***b* = -1.62, *p* = .035**	*b* = 0.07, *p* = .228 *b* = 0.02, *p* = .280 *b* = -0.04, *p* = .079 *b* = 0.18, *p* = .357	***b* = 1.83, *p* <.001** ***b* = 0.70, *p* <.001** ***b* = -0.49, *p* <.001** *b* = 1.85, *p* = .075	***b* = 1.95, *p* <.001** ***b* = 0.74, *p* <.001** ***b* = -0.55, *p* <.001** ***b* = 2.15, *p* = .049**	*b* = 0.11, CI [-0.40, 0.14] *b* = -0.03, CI [-0.15, 0.02] *b* = 0.06, CI [-0.01, 0.20] *b* = -0.31, CI [-1.51, 0.68]
ADAPSS Negativity	Life Interference Distress Life Control MPICa	***b* = -0.43, *p* = .037**	*b* = 0.01, *p* = .866 *b* = -.001, *p* = .969 *b* = -.001, *p* = .975 *b* = 0.03, *p* = .688	***b* = 0.50, *p* <.001** ***b* = 0.14, *p* <.001** ***b* = -0.15, *p* <.001** ***b* = -0.30, *p* = .041**	***b* = 0.51, *p* <.001** ***b* = 0.14, *p* <.001** ***b* = -0.15, *p* <.001** *b* = -0.28, *p* = .060	*b* = -0.003, CI [-0.07, 0.05] *b* = .0003, CI [-0.02, 0.02] *b* = .0002, CI [-0.01,

	MPICb		*b* = 0.10, *p* = .487	***b* = 0.91, *p* <.001**	***b* = 0.96, *p* <.001**	0.004] *b* = -0.01, CI [0.12, 0.09] *b* = -0.04, CI [-0.37, 0.13]
ADAPSS Resilience	Life Interference Distress Support Life Control MPICa	***b* = 0.85, *p* = .002**	*b* = -0.02, *p* = .774 *b* = 0.01, *p* = .560 ***b* = 0.05, *p* = .025** *b* = -0.01, *p* = .467 *b* = -0.02, *p* = .810	***b* = -0.32, *p* = .014** ***b* = -0.20, *p* <.001** ***b* = 0.13, *p* = .014** ***b* = 0.21, *p* <.001** ***b* = 0.61, *p* = .002**	***b* = -0.30, *p* = .028** ***b* = -0.21, *p* <.001** *b* = 0.08, *p* = .112 ***b* = 0.22, *p* <.001** ***b* = 0.62, *p* = .003**	*b* = -0.01, CI [-0.16, 0.10] *b* = 0.01, CI [-0.02, 0.04] b = 0.04, CI [-0.003, 0.09] *b* = -0.01, CI [-0.05, 0.03] *b* = -0.02, CI [-0.18, 0.15]
Pain Catastrophizing	Pain Intensity Life Interference Distress Support Life Control MPICb	***b* = -0.50, *p* = .015**	***b* = 0.02, *p* = .045** *b* = 0.01, *p* = .851 *b* = 0.0004, *p* = .984 ***b* = 0.07, *p* = .002** *b* = -0.001, *p* = .935 *b* = 0.10, *p* = .508	***b* = 0.05, *p* = .003** ***b* = 0.45, *p* <.001** ***b* = 0.13, *p* <.001** *b* = 0.01, *p* = .843 ***b* = -0.14, *p* <.001** ***b* = 0.78, *p* = .004**	***b* = 0.06, *p* <.001** ***b* = 0.45, *p* <.001** ***b* = 0.13, *p* <.001** *b* = 0.04, *p* = .276 ***b* = -0.14, *p* <.001** ***b* = 0.83, *p* = .003**	*b* = -0.01, CI [-0.02, 0.001] *b* = -0.004, CI [-0.05, 0.07] *b* = -.0002, CI [-0.02, 0.02] ***b* = -0.03, CI [-0.06, -.001]** *b* = 0.001, CI [-0.02, 0.03] *b* = -0.05, CI [-0.31, 0.19]
Anxiety	Life Interference Distress Life Control MPICb	*b* = -0.49, *p* = .386	*b* = -0.04, *p* = .427 *b* = -0.01, *p* = .559 *b* = 0.01, *p* = .489 *b* = 0.01, *p* = .965	***b* = 1.12, *p* <.001** ***b* = 0.51, *p* <.001** ***b* = -0.40, *p* <.001** ***b* = 1.63, *p* = .025**	***b* = 1.10, *p* <.001** ***b* = 0.50, *p* <.001** ***b* = -0.40, *p* <.001** ***b* = 1.64, *p* = .026**	*b* = 0.02, CI [-0.06, 0.14] *b* = 0.01, CI [-0.02, 0.03] *b* = -0.01, CI [-0.05, 0.03] *b* = -0.003, CI [-0.40, 0.30]
Mental Defeat	Pain Intensity Life Interference Distress Support Life Control	***b* = -0.22, *p* = .028**	*b* = 0.02, *p* = .056 *b* = -0.002, *p* = .971 *b* = -0.0004, *p* = .984 ***b* = 0.07, *p* = .001** *b* = 0.001, *p* = .973	***b* = 0.02, *p* = .003** ***b* = 0.20, *p* <.001** ***b* = 0.07, *p* <.001** *b* = 0.01, *p* = .604 ***b* = -0.06, *p* <.001**	***b* = 0.03, *p* <.001** ***b* = 0.20, *p* <.001** ***b* = 0.07, *p* <.001** *b* = 0.02, *p* = .176 ***b* = 0.06, *p* <.001**	*b* = -0.004, CI [-0.01, .001] *b* = .0004, CI [-0.02, 0.03] *b* = .0001, CI [-0.01, 0.01] ***b* = -0.02, CI [-0.03, -.001]** *b* = -.0001, CI [-0.01, 0.01]
Stress	Life Interference Distress Support	***b* = -0.74, *p* = .038**	*b* = -0.02, *p* = .677 *b* = 0.004, *p* = .793 ***b* = 0.06, *p* = .004**	***b* = 0.53, *p* = .001** ***b* = 0.31, *p* <.001** *b* = -0.02, *p* = .740	***b* = 0.51, *p* = .003** ***b* = 0.32, *p* <.001** *b* = 0.03, *p* = .706	*b* = 0.02, CI [-0.09, 0.13] *b* = -0.003, CI [-0.03, 0.02]

	Life Control		*b* = -0.001, *p* = .951	***b* = -0.27, *p* <.001**	***b* = -0.27, *p* <.001**	***b* = -0.05, CI [-0.12, -.001]** *b* = 0.001, CI [-0.07, 0.06]
Negative Response	Life Interference Distress	*b* = -0.65, *p* = .137	*b* = -0.04, *p* = .497 *b* = -0.01, *p* = .572	***b* = 0.58, *p* = .004** ***b* = 0.20, *p* = .006**	***b* = 0.55, *p* = .007** ***b* = 0.19, *p* = .010**	*b* = 0.02, CI [-0.09, 0.13] *b* = 0.01, CI [-0.03, 0.04]
Distracting Response	Support	*b* = 0.69, *p* = .137	***b* = 0.04, *p* = .011**	***b* = 0.46, *p* <.001**	***b* = 0.43, *p* <.001**	*b* = 0.03, CI [-0.01, 0.09]
Solicitous Response	Support	*b* = 0.19, *p* = .609	***b* = 0.06, *p* = .002**	***b* = 0.32, *p* <.001**	***b* = 0.31, *p* <.001**	*b* = 0.01, CI [-0.04, 0.07]

Note: The confidence intervals for the indirect effect is a BCa bootstrapped CI based on 5000 samples. Significant results are shown in bold print.

Mediator: ADAPSS Catastrophic Negativity & Resilience



Predictor	Outcome	ai Negativity aii Resilience	bi Negativity bii Resilience	c	Direct	Indirect Total Indirect Negativity Indirect Resilience
Mental Defeat	Pain Intensity	***b* = 0.36, *p* <.001** ***b* = -0.17, *p* <.001**	*b* = -0.02, *p* = .358 *b* = 0.04, *p* = .148	***b* = 0.02, *p* = .003**	***b* = 0.04, *p* = .002**	*b* = -0.01, CI [-0.03, 0.002] *b* = -0.01, CI [-0.02, 0.01]

						b = -0.01, CI [-0.02, .0004]
	Life Interference		***b* = 0.43, *p* <.001** *b* = -0.02, *p* = .871	***b* = 0.20, *p* <.001**	*b* = 0.05, *p* = .438	***b* = 0.16, CI [0.09, 0.23]** ***b* = 0.15, CI [0.10, 0.23]** *b* = 0.003, CI [-0.04, 0.04]
	Distress		*b* = 0.07, *p* = .099 ***b* = -0.14, *p* = .004**	***b* = 0.07, *p* <.001**	*b* = 0.02, *p* = .432	***b* = 0.05, CI [0.02, 0.08]** ***b* = 0.03, CI [0.0008, 0.06]** ***b* = 0.02, CI [0.004, 0.04]**
	Life Control		***b* = -0.09, *p* = .022** ***b* = 0.15, *p* <.001**	***b* = -0.07, *p* <.001**	*b* = -0.01, *p* = .706	***b* = -0.06, CI [-0.09, -0.03]** ***b* = -0.03, CI [-0.06, -0.01]** ***b* = -0.02, CI [-0.04, -0.01]**
	MPICa		*b* = -0.26, *p* = .216 ***b* = 0.58, *p* = .008**	*b* = -0.10, *p* = .164	*b* = 0.09, *p* = .387	***b* = -0.19, CI [-0.35, -0.03]** *b* = -0.09, CI [-0.26, 0.06] ***b* = -0.10, CI [-0.17, -0.03]**
	MPICb		***b* = 1.27, *p* = .001** *b* = 0.20, *p* = .597	*b* = 0.23, *p* = .082	*b* = -0.19, *p* = .309	***b* = 0.42, CI [0.15, 0.70]** ***b* = 0.45, CI [0.21, 0.73]** *b* = -0.03, CI [-0.22, 0.07]
Stress	Life Interference	***b* = 0.95, *p* <.001** ***b* = -0.84, *p* <.001**	***b* = 0.48, *p* <.001** *b* = -0.02, *p* = .867	***b* = 0.53, *p* = .001**	*b* = 0.05, *p* = .798	***b* = 0.48 CI [0.20, 0.82]** ***b* = 0.46, CI [0.24, 0.78]** *b* = 0.02, CI [-0.17, 0.20]
	Distress		*b* = 0.06, *p* = .082 *b* = -0.07, *p* = .194	***b* = 0.31, *p* <.001**	***b* = 0.20, *p* = .005**	***b* = 0.11, CI [0.01, 0.21]** *b* = 0.06, CI [-0.001, 0.15] *b* = 0.05, CI [-0.04, 0.13]
	Support		*b* = 0.04, *p* = .338 ***b* = 0.20, *p* = .003**	*b* = -0.02, *p* = .740	*b* = 0.12, *p* = .245	*b* = -0.13 CI [-0.26, 0.01] *b* = 0.04, CI [-0.04, 0.19] ***b* = -0.17, CI [-0.30, -0.06]**
	Life Control		***b* = -0.09, *p* = .008** ***b* = 0.11, *p* = .018**	***b* = -0.27, *p* <.001**	*b* = -0.09, *p* = .160	***b* = -0.18, CI [-0.28, -0.08]** ***b* = -0.08, CI [-0.16, -0.03]** *b* = -0.09, CI [-0.17, -0.03]
	MPICa		*b* = -0.21, *p* = .213 ***b* = 0.68, *p* = .007**	*b* = -0.39, *p* = .133	*b* = 0.38, *p* = .279	***b* = -0.76, CI [-1.30, -0.32]** *b* = -0.20, CI [-0.61, 0.08] ***b* = -0.57, CI [-1.01, -0.16]**

	MPICb		***b* = 1.18, *p* <.001** *b* = -0.04, *p* = .922	*b* = 0.25, *p* = .596	*b* = -0.90, *p* = .153	***b* = 1.15, CI [0.25, 2.20]** ***b* = 1.12, CI [0.49, 1.97]** *b* = 0.04, CI [-0.76, 0.78]
Pain Catastrophizing	Pain Intensity	***b* = 0.71, *p* <.001** ***b* = -0.30, *p* <.001**	*b* = -0.01, *p* = .524 *b* = 0.03, *p* = .256	***b* = 0.05, *p* = .003**	***b* = 0.07, *p* = .004**	*b* = -0.02, CI [-0.05, 0.01] *b* = -0.01, CI [-0.04, 0.02] *b* = -0.01, CI [-0.03, 0.01]
	Life Interference		***b* = 0.38, *p* <.001** *b* = -0.01, *p* = .920	***b* = 0.45, *p* <.001**	*b* = 0.18, *p* = .114	***b* = 0.27, CI [0.12, 0.44]** ***b* = 0.27, CI [0.12, 0.44]** *b* = 0.003, CI [-0.08, 0.06]
	Distress		*b* = 0.07, *p* = .084 ***b* = -0.14, *p* = .003**	***b* = 0.13, *p* <.001**	*b* = 0.04, *p* = .397	***b* = 0.09, CI [0.04, 0.15]** ***b* = 0.05, CI [0.0001, 0.12]** ***b* = 0.04, CI [0.01, 0.07]**
	Support		*b* = 0.05, *p* = .373 ***b* = 0.17, *p* = .004**	*b* = 0.01, *p* = .843	*b* = 0.02, *p* = .660	*b* = -0.02, CI [-0.09, 0.07] *b* = 0.03, CI [-0.04, 0.13] ***b* = -0.05, CI [-0.12, -0.01]**
	Life Control		***b* = -0.08, *p* = .037** ***b* = 0.14, *p* <.001**	***b* = -0.14, *p* <.001**	*b* = -0.04, *p* = .353	***b* = -0.10, CI [-0.16, -0.04]** ***b* = -0.06, CI [-0.11, -0.01]** ***b* = -0.04, CI [-0.07, -0.02]**
	MPICa		*b* = -0.15, *p* = .440 ***b* = 0.54, *p* = .013**	*b* = -0.24, *p* = .105	*b* = 0.03, *p* = .885	*b* = -0.27, CI [-0.65, 0.07] *b* = -0.11, CI [-0.49, 0.20] ***b* = -0.16, CI [-0.27, -0.04]**
	MPICb		***b* = 0.81, *p* = .028** *b* = 0.36, *p* = .340	***b* = 0.78, *p* = .004**	*b* = 0.31, *p* = .391	*b* = 0.47, CI [-0.04, 1.07] ***b* = 0.58, CI [0.07, 1.23]** *b* = -0.11, CI [-0.43, 0.11]
Acceptance	Distress	***b* = -0.14, *p* = .037** ***b* = 0.15, *p* = .002**	***b* = 0.10, *p* = .003** ***b* = -0.16, *p* = .001**	*b* = -0.02, *p* = .321	*b* = 0.02, *p* = .343	***b* = -0.04, CI [-0.07, -0.01]** *b* = -0.01, CI [-0.04, .0003] ***b* = -0.02, CI [-0.04, -.005]**
	Support		*b* = 0.07, *p* = .065 ***b* = 0.12, *p* = .031**	***b* = 0.06, *p* = .003**	***b* = 0.05, *p* = .014**	*b* = 0.01, CI [-0.01, 0.04] *b* = -0.01, CI [-0.04, 0.003] *b* = 0.02, CI [-0.001, 0.06]

	Life Control		***b* = -0.12, *p* <.001** ***b* = 0.16, *p* <.001**	*b* = 0.02, *p* = .298	*b* = -0.02, *p* = .238	***b* = 0.04, CI [0.01, 0.07]** *b* = 0.01, CI [-0.001, 0.04] ***b* = 0.02, CI [0.01, 0.04]**
	MPICa		*b* = -0.14, *p* = .358 ***b* = 0.55, *p* = .013**	*b* = 0.07, *p* = .386	*b* = -0.03, *p* = .734	***b* = 0.10, CI [0.03, 0.21]** *b* = 0.02, CI [-0.02, 0.11] ***b* = 0.08, CI [0.01, 0.17]**
Anxiety	Life Interference	***b* = 1.50, *p* <.001** ***b* = -0.68, *p* = .003**	***b* = 0.40, *p* <.001** *b* = -0.01, *p* = .949	***b* = 1.12, *p* <.001**	***b* = 0.52, *p* = .040**	***b* = 0.60, CI [0.33, 0.89]** ***b* = 0.59, CI [0.34, 0.90]** *b* = 0.005, CI [-0.15, 0.13]
	Distress		*b* = 0.03, *p* = .394 ***b* = -0.12, *p* = .004**	***b* = 0.51, *p* <.001**	***b* = 0.38, *p* <.001**	***b* = 0.13, CI [0.02, 0.26]** *b* = 0.04, CI [-0.04, 0.15] ***b* = 0.08, CI [0.01, 0.17]**
	Support		*b* = 0.07, *p* = .146 ***b* = 0.16, *p* = .005**	*b* = -0.04, *p* = .720	*b* = -0.03, *p* = .803	*b* = -0.01, CI [-0.17, 0.18] *b* = 0.10, CI [-0.05, 0.33] ***b* = -0.12, CI [-0.28, -0.01]**
	Life Control		***b* = -0.06, *p* = .046** ***b* = 0.14, *p* <.001**	***b* = -0.40, *p* <.001**	***b* = -0.21, *p* = .014**	***b* = -0.19, CI [-0.33, -0.07]** ***b* = -0.10, CI [-0.20, -0.01]** ***b* = -0.09, CI [-0.17, -0.02]**
	MPICa		*b* = 0.12, *p* = .479 ***b* = 0.53, *p* = .014**	*b* = -0.61, *p* = .124	*b* = -0.07, *p* = .883	*b* = -0.55, CI [-1.25, 0.05] *b* = -0.19, CI [-0.80, 0.36] ***b* = -0.36, CI [-0.77, -0.04]**
	MPICb		***b* = 0.92, *p* = .005** *b* = 0.34, *p* = .370	***b* = 1.63, *p* = .025**	*b* = 0.49, *p* = .555	***b* = 1.14, CI [0.17, 2.35]** ***b* = 1.37, CI [0.36, 2.54]** *b* = -0.23, CI [-0.93, 0.32]
Depression	Life Interference	***b* = 1.85, *p* <.001** ***b* = -0.95, *p* <.001**	***b* = 0.38, *p* = .002** *b* = 0.15, *p* = .367	***b* = 1.83, *p* <.001**	***b* = 1.27, *p* <.001**	***b* = 0.57, CI [0.02, 1.11]** ***b* = 0.71, CI [0.30, 1.16]** *b* = -0.14, CI [-0.54, 0.10]
	Distress		*b* = 0.05, *p* = .251 ***b* = -0.13, *p* = .029**	***b* = 0.70, *p* <.001**	***b* = 0.50, *p* <.001**	***b* = 0.20, CI [0.02, 0.38]** *b* = 0.08, CI [-0.05, 0.25] ***b* = 0.12, CI [0.01, 0.23]**
	Support		***b* = 0.17, *p* = .009** ***b* = 0.24, *p* = .008**	*b* = -0.11, *p* = .478	*b* = -0.20, *p* = .313	*b* = 0.08, CI [-0.24, 0.42] ***b* = 0.31, CI [0.08, 0.60]** ***b* = -0.23, CI [-0.41, -0.05]**

	Life Control		***b* = -0.09, *p* = .042** *b* = 0.12, *p* = .061	***b* = -0.49, *p* <.001**	*b* = -0.21, *p* = .134	***b* = -0.28, CI [-0.48, -0.07]** ***b* = -0.17, CI [-0.33, -0.02]** *b* = -0.11, CI [-0.21, 0.003]
	MPICa		*b* = 0.02, *p* = .924 ***b* = 0.081, *p* = .016**	*b* = -0.71, *p* = .198	*b* = 0.01, *p* = .985	*b* = -0.73,CI [-1.69, 0.42] *b* = 0.04, CI [-0.68, 0.97] ***b* = -0.76, CI [-1.39, -0.20]**
Distracting Response	Life Interference	*b* = -0.03, *p* = .895 ***b* = 0.48, *p* = .012**	***b* = 0.47, *p* <.001** *b* = -0.12, *p* = .299	*b* = 0.32, *p* = .139	***b* = 0.39, *p* = .030**	*b* = -0.07, CI [-0.39, 0.21] *b* = -0.02, CI [-0.27, 0.23] *b* = -0.06, CI [-0.20, 0.04]
	Distress		***b* = 0.09, *p* = .006** ***b* = -0.16, *p* <.001**	*b* = 0.01, *p* = .857	*b* = 0.10, *p* = .171	*b* = -0.08, CI [-0.20, 0.02] *b* = -0.003, CI [-0.07, 0.05] ***b* = -0.08, CI [-0.17, -0.01]**
	Support		*b* = 0.04, *p* = .249 *b* = 0.07, *p* = .119	***b* = 0.46, *p* <.001**	***b* = 0.43, *p* <.001**	*b* = 0.03, CI [-0.03, 0.12] *b* = -0.001, CI [-0.04, 0.04] *b* = 0.04, CI [-0.02, 0.13]
	Life Control		***b* = -0.10, *p* <.001** ***b* = 0.15, *p* <.001**	*b* = 0.07, *p* = .372	*b* = -0.01, *p* = .897	*b* = 0.08, CI [-0.02, 0.17] *b* = 0.003, CI [-0.05, 0.06] ***b* = 0.07, CI [0.01, 0.14]**
	MPICa		*b* = -0.15, *p* = .337 ***b* = 0.49, *p* = .028**	*b* = 0.46, *p* = .166	*b* = 0.22, *p* = .501	*b* = 0.24, CI [-0.03, 0.55] *b* = 0.01, CI [-0.10, 0.18] ***b* = 0.23, CI [0.01, 0.51]**
Negative Response	Life Interference	***b* = 0.48, *p* = .051** ***b* = -0.52, *p* = .003**	***b* = 0.47, *p* <.001** *b* = 0.02, *p* = .838	***b* = 0.58, *p* = .004**	***b* = 0.36, *p* = .037**	***b* = 0.21, CI [0.02, 0.47]** ***b* = 0.23, CI [0.02, 0.50]** *b* = -0.01, CI [-0.14, 0.08]
	Distress		***b* = 0.09, *p* = .005** ***b* = -0.13, *p* = .006**	***b* = 0.20, *p* = .006**	*b* = 0.09, *p* = .180	***b* = 0.11, CI [0.04, 0.21]** ***b* = 0.04, CI [0.004, 0.12]** ***b* = 0.07, CI [0.01, 0.15]**
	Support		*b* = 0.07, *p* = .112 ***b* = 0.15, *p* = .010**	*b* = -0.12, *p* = .189	*b* = -0.06, *p* = .470	*b* = -0.05, CI [-0.13, 0.03] *b* = 0.03, CI [-0.01, 0.14] ***b* = -0.08, CI [-0.19, -.003]**

	Life Control		***b* = -0.10, *p* <.001** ***b* = 0.15, *p* <.001**	*b* = -0.14, *p* = .055	*b* = -0.01, *p* = .869	***b* = -0.13, CI [-0.24, -0.05]** ***b* = -0.05, CI [-0.12, -0.01]** ***b* = -0.08, CI [-0.16, -0.02]**
	MPICa		*b* = -0.15, *p* = .328 ***b* = 0.58, *p* = .008**	*b* = -0.09, *p* = .776	*b* = 0.28, *p* = .366	***b* = -0.37, CI [-0.78, -0.11]** *b* = -0.07, CI [-0.33, 0.09] ***b* = -0.30, CI [-0.65, -0.06]**
	MPICb		***b* = 0.99, *p* <.001** *b* = 0.37, *p* = .340	*b* = 0.63, *p* = .273	*b* = 0.35, *p* = .535	*b* = 0.28, CI [-0.20, 0.95] ***b* = 0.47, CI [0.03, 1.30]** *b* = -0.19, CI [-0.68, 0.19]
Solicitous Response	Support	*b* = 0.12, *p* = .570 *b* = 0.11, *p* = .471	*b* = 0.04, *p* = .229 ***b* = 0.13, *p* = .007**	***b* = 0.32, *p* <.001**	***b* = 0.30, *p* <.001**	*b* = 0.02, CI [-0.02, 0.08] *b* = 0.01 CI [-0.02, 0.04] *b* = 0.01, CI [-0.02, 0.08]

Note: The confidence intervals for the indirect effect is a BCa bootstrapped CI based on 5000 samples. Significant results are shown in bold print.

16 Appendix 4 – Correlation Tables

Age and Biopsychosocial Variables – In-Patients

	1	2	3	4	5	6	7	8	9	10	11	12	13
1. T1LANSS	1												
2. T1PSS	-.14	1											
3. T1PCS	-.02	.62**	1										
4. T1ADAPSSNegativity	.05	.64**	.64**	1									
5. T1ADAPSSresilience	.22	-.55**	-.54**	-.58**	1								
6. T1PSPS	-.09	.57**	.63**	.71**	-.37**	1							
7. T1CPAQ	.07	-.43**	-.64**	-.62**	.55**	-.55**	1						
8. T1DepScore	.02	.74**	.72**	.75**	-.57**	.74**	-.56**	1					
9. T1AnxScore	.09	.65**	.64**	.62**	-.22	.58**	-.37**	.75**	1				
10. T1MPIBdistracting	.09	.02	-.03	.12	.22	.17	.02	.09	.14	1			
11. T1MPIBnegative	-.09	.23	.26*	.19	-.18	.34**	-.32*	.30*	.09	-.02	1		
12. T1MPIBsolicitous	.09	-.05	-.17	.11	.18	.14	-.04	.08	.17	.42**	-.06	1	
13. Age	-.03	-.11	-.26*	-.17	.02	-.17	.11	-.12	-.22	-.24	-.09	-.15	1

** Correlation is significant at the 0.01 level (2-tailed).

* Correlation is significant at the 0.05 level (2-tailed).

Unless otherwise noted, bootstrap results are based on 1000 bootstrap samples

Age and Biopsychosocial Variables – Out-Patients

	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19
1. Age	1																		
2. LANSS	-.02	1																	
3. PSS	-.09	.23	1																
4. PCS	-.06	.16	.63**	1															
5. ADAPSS Negativity	.13	.15	.63**	.74**	1														
6. ADAPSS Resilience	-.21	.01	-.62**	-.39*	-.38*	1													
7. PSPS	-.01	.22	.61**	.85**	.85**	-.35*	1												
8. CPAQ	.09	-.15	-.29	-.28	-.15	.38*	-.21	1											
9. DepScore	.08	.26	.63**	.71**	.63**	-.49**	.77**	-.34*	1										
10. AnxScore	.16	.19	.67**	.72**	.72**	-.45**	.79**	-.13	.78**	1									
11. MPIBdistracting	-.26	-.07	.04	.20	.13	.34*	.24	.09	.09	.15	1								
12. MPIBnegative	.16	.18	.37*	.37*	.39*	-.41**	.30	-.45**	.34*	.34*	-.16	1							
13. MPIBsolicitous	-.17	-.14	.13	.22	.21	.05	.28	-.11	-.00	.18	.65**	.15	1						
14. MPILifeInterfere	.22	.18	.40**	.63**	.69**	-.30	.68**	-.22	.74**	.66**	.19	.45**	.15	1					
15. MPISupport	-.05	-.04	-.05	.01	.14	.41**	.15	.23	-.11	.09	.69**	-.24	.66**	.08	1				
16. MPILifeControl	-.01	-.17	-.59**	-.59**	-.54**	.48**	-.54**	.01	-.58**	-.61**	.02	-.13	.03	-.51**	.15	1			
17. MPIPainSeverity	-.12	.30	.22	.56**	.42**	-.19	.60**	-.18	.57**	.47**	.17	.19	.15	.55**	-.03	-.48**	1		
18. MPIDistress	.01	.17	.75**	.58**	.56**	-.56**	.56**	-.22	.75**	.73**	.09	.33*	.00	.58**	-.18	-.62**	.41**	1	
19. MPIC	-.32*	.06	-.05	-.13	-.13	.39**	-.13	.09	-.18	-.13	.23	-.04	-.06	-.17	.21	.32*	-.04	-.15	1

* Correlation is significant at the 0.05 level (2-tailed).

** Correlation is significant at the 0.01 level (2-tailed).

Unless otherwise noted, bootstrap results are based on 1000 bootstrap samples

Cortisol and biopsychosocial variables - In-Patients T3 and Out-Patients combined

	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19
1. MPIBdis	1																		
2. MPIBneg	.05	1																	
3. MPIBsol	.54**	.23*	1																
4. PCStotal	.13	.24*	.15	1															
5. ADAPSneg	.04	.28*	.11	.51**	1														
6. ADAPSres	.27*	-.24*	.01	-.21*	-.27*	1													
7. PSPStot	.13	.16	.20	.63**	.61**	-.25*	1												
8. CPAQtot	.09	-.17	.02	-.11	-.11	.18	-.09	1											
9. HADSDep	.05	.14	.02	.43**	.41**	-.29**	.52**	-.23*	1										
10. HADSAnx	.07	.26*	.09	.49**	.56**	-.31**	.53**	-.09	.62**	1									
11. PSStotal	-.00	.23*	.05	.45**	.50**	-.45**	.45**	-.19	.47**	.51**	1								
12. MPICTot	.06	-.08	-.12	-.10	-.13	.32**	-.13	.02	-.10	-.13	-.12	1							
13. MPIAli	.18	.37**	.19	.46**	.48**	-.20	.44**	-.13	.48**	.51**	.30**	-.15	1						
14. MPIASupp	.54**	.00	.50**	.20	.24*	.17	.27*	.18	.06	.16	.06	-.01	.29**	1					
15. MPIACont	.03	-.13	.01	-.40**	-.37**	.27*	-.29**	.02	-.37**	-.41**	-.41**	.26*	-.34**	-.04	1				
16. MPIPainSeverity	.11	.20	.18	.39**	.25*	-.07	.37**	-.15	.32**	.30**	.11	-.10	.43**	.15	-.29**	1			
17. MPIAdis	.08	.28*	.07	.33**	.38**	-.34**	.32**	-.09	.50**	.56**	.54**	-.16	.47**	.09	-.43**	.28*	1		
18. T1LANSStotal	-.02	.04	-.09	.15	.14	.07	.21	-.15	.19	.14	.15	-.01	.15	.03	-.10	.22*	.15	1	
19. Cortisol	.13*	.06	-.00	.18**	.04	.10	.16	-.03	.13	.10	.15*	-.07	.07	.04	.02	.14	.07	.04	1

** Correlation is significant at the 0.01 level (2-tailed).

* Correlation is significant at the 0.05 level (2-tailed).

Unless otherwise noted, bootstrap results are based on 1000 bootstrap samples

Time since injury and biopsychosocial variables – In-Patients and Out-Patients combined

	1	2	3	4	5	6	7	8	9	10	11	12	13
1. MPIBdis	1												
2. MPIBneg	.06	1											
3. PCStotal	.16	.33*	1										
4. PSPStot	.18	.19	.80**	1									
5. CPAQPainWillingness	-.03	-.29	-.14	-.16	1								
6. HADSDep	.08	.18	.59**	.68**	-.26	1							
7. HADSAnx	.10	.35*	.66**	.72**	-.06	.77**	1						
8. PSStotal	.00	.30	.61**	.59**	-.17	.61**	.65**	1					
9. Cortisol	.15	.07	.34*	.22	-.04	.35*	.25	.14	1				
10. TimeInjuredDays	-.20*	.09	.28	.19*	-.00	.19	.13	.15	-.34**	1			
11. PCSruminate	.12	.19	.93**	.77**	-.15	.58**	.55**	.54**	.35*	.18	1		
12. PCSmagnify	.21	.45**	.79**	.66**	-.19	.44**	.65**	.49**	.22	.27	.65**	1	
13. PCShelplessness	.14	.26	.96**	.76**	-.08	.56**	.60**	.57**	.34*	.25**	.89**	.67**	1

* Correlation is significant at the 0.05 level (2-tailed).

** Correlation is significant at the 0.01 level (2-tailed).

Unless otherwise noted, bootstrap results are based on 1000 bootstrap samples

Time since injury and biopsychosocial variables – In-Patients

		4	5	7	12	13
1.	T1ADAPSScatNegativitytotal	1				
2.	T1ADAPSSresiliencetotal	-.58**	1			
3.	T1CPAQtotal	-.62**	.55**	1		
4.	T1MPIBsolicitous	.11	.18	-.04	1	
5.	TimeInjuredDays	-.09	-.10	.04	-.2	1

** Correlation is significant at the 0.01 level (2-tailed).

* Correlation is significant at the 0.05 level (2-tailed).

Unless otherwise noted, bootstrap results are based on 1000 bootstrap samples

Time since injury and biopsychosocial variables – Out-Patients

		4	5	7	12	19
1.	ADAPSS Negativity	1				
2.	ADAPSS Resilience	-.38*	1			
3.	CPAQ	-.15	.38*	1		
4.	MPIBsolicitous	.20	.04	-.11	1	
5.	TimeInjuredDays	.28	-.10	.00	-.03	1

** Correlation is significant at the 0.01 level (2-tailed).

* Correlation is significant at the 0.05 level (2-tailed).

Unless otherwise noted, bootstrap results are based on 1000 bootstrap samples

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