Theoretical Basis of Pain

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Abstract

Pain experiences, both acute and chronic, are common in infants, children, and adolescents. The aim of this chapter is to give an overview of different biopsychosocial paediatric pain models that address acute or chronic pain. Recent insights in neural processes are discussed, as well as psychosocial mechanisms across a child's development. The crucial role of parents in different theoretical conceptualizations is highlighted. We emphasize that both risk factors for the development of chronic pain-related disability and resilience mechanisms for adaptive child functioning should be considered.

Keywords: pain, infant, child, parent, biopsychosocial, theory, risk, resilience

Introduction

Pain is a common experience in childhood and adolescence. Although the majority of pain complaints in children are short lasting and only temporarily disabling, a significant number of children do not recover within a reasonable span of time (Petersen et al. 2006). Chronic and recurrent pain is prevalent in children and adolescents, with median prevalence rates ranging from 11% to 38% (King et al. 2011). Most children seem to function well despite pain, although a minority (5 - 14%) are moderately or severely disabled across several domains of functioning (Huguet & Miró 2008; Vervoort et al. 2014).

Infants that are born prematurely have to undergo an average of 8 - 16 painful procedures a day within the Neonatal Intensive Care Unit (Britto et al., 2014). Children with medical conditions (e.g., cancer) experience frequent diagnostic and therapeutic procedures that are often painful. Even healthy children are exposed to significant amounts of painful medical procedures throughout childhood. For example, countries that have established vaccination programs often prescribe upwards of 20 vaccine needles over the first 5 years of life (https://www.cdc.gov/vaccines/hcp/vis/vis-statements/multi.html). Thus, pain is an unavoidable aspect of childhood that can impact how children process pain as adults. These examples necessitate a solid understanding of pain from a comprehensive, multidisciplinary perspective.

Since the proposal of the Gate Control Theory by Patrick Wall and Ronald Melzack in 1965, pain has been conceptualized as a biopsychosocial phenomenon, reflected in the definition by the International Association for the Study of Pain as "*an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage*" (Bonica 1979, p. 250). However, the social dimensions of pain, particularly important in the context of childhood pain, have received less attention in comparison to the biological and psychological dimensions. In 2016, Williams and Craig (2016, p. 2420) proposed a new definition of pain that more strongly emphasized the social and psychological dimensions: *"Pain is a distressing experience associated with actual or potential tissue damage with sensory, emotional, cognitive, and social components"*.

This chapter outlines different theoretical perspectives on acute and chronic paediatric pain as a biopsychosocial phenomenon across childhood, with a focus on psychosocial aspects. The chapter will begin with a discussion of the biological underpinnings of pain modulation- which is a biopsychosocial phenomenon that epitomizes the multidimensional nature of pain. We will then discuss evidence-based theories of paediatric pain that postulate biopsychosocial mechanisms, often involving modulation or regulation of the pain response. Finally, clinical implications and a conclusion will be outlined to suggest conceptual directions for integrated models of paediatric pain.

The Modulation of Pain

A Brief History

In a ground-breaking report published in 1969 in Science, electrical stimulation of the periaqueductal gray (PAG) was shown to induce analgesia (Reynolds et al. 1969).

Subsequently the circuitry of endogenous pain modulation was defined (Basbaum and Fields, 1978). The idea of pain facilitation or inhibition has been supported by numerous preclinical studies (Millan, 2002; Silva et al., 2013; Porreca et al., 2002). The concept of endogenous modulation of pain took a number of years to be further defined in humans. The ramifications have been huge – from improved understanding of placebo (Benedetti 2007) or nocebo (Gueter and Buchel, 2013) to altered endogenous modulation (facilitation or inhibition) in chronic pain states (Hemington and Coulombe, 2015). A complex network that includes forebrain and subcortical areas that have input into brainstem regions, most notably the PAG and raphe magnus (RM), provides a basis for descending modulatory controls.

Evidence in Humans

Endogenous Factors associated with Pain Modulation

In humans a number of interventions added to the clinical relevance and therapeutic importance of endogenous modulation of pain. In its effective state – pain is inhibited, but when deficient, pain may be exacerbated. Some surgical procedures provided some insights into human pain – cingulotomies (i.e., removal of the cingulate) have reportedly alleviated pain through complex mechanisms that may involve decreased attention or altered pain affect (Vizwanathan et al., 2013). Deep brain stimulation for pain control has been used since the 1970's and have included areas known to be involved in pain modulation (e.g., Anterior Cingulate Cortex or PAG). However, paediatric studies are limited.

Exogenous Factors associated with Pain Modulation

A summary of exogenous factors associated with pain modulation may be considered in three groups: (a) Pharmacological modulation, (b) Neural modulation, and (c) Psychological modulation.

Pharmacological Modulation - Drugs may alter or restore decreased inhibitory controls (Zeilhofer et al., 2012). Many pharmacological agents act on regions involved in descending modulation. For example, tapentadol or ketamine are thought to potentiate descending analgesia in patients with neuropathic pain (Niesters et al., 2013; 2014), while other agents (buprenorphine or fentanyl) enhance this mechanism in experimental human pain (Arendt-Nielson et al., 2012). What is unclear is how pharmacological agents may continue to drive inhibitory or inhibit facilitatory descending modulatory processes in chronic pain where the evidence for chronic dosing is not very well established. Very little information is available in children but can be extrapolated from adult experiments because of the robust conservation of biological pathways.

Neural Modulation – Neural modulators have become an interesting approach to chronic pain. Early work involved cortical stimulation of somatosensory/motor regions (Tsubokawa et al., 1991) or direct placement of electrodes into the PAG (Hosobuchi et al., 1979). More recently neuromodulation via transcranial magnetic stimulation (TMS) has been deployed for chronic pain control (O'Connell et al., 2014). We are unaware of any studies of the use of TMS or other neuromodulation in treating pain in children,

although such approaches have been used in child and adolescent psychiatry (Croarkin et al., 2011).

Psychological modulation - While major neural pathways involved in pain modulation are quite well understood, the manipulation of endogenous analgesia has mostly focused on healthy subjects with fewer studies in the clinical population. With respect to the former, various techniques such as Cognitive Behavior Therapy or other techniques affecting cognitive processes such as meditation (Sharon et al., 2016) or placebo (Schmid et al., 2015) have been used to enhance endogenous pain control. Various methods to enhance such approaches such as virtual reality have recently been deployed in children and adults to enhance acute pain modulation (Arane et al., 2017).

There are several cognitive and behavioural models of pain to further our understanding of childhood pain experience, pain behaviours, and pain-related functioning. First, a general biopsychosocial framework will be presented that has often been applied for understanding the complexities of human pain communication and pain-related interactions, by drawing from different perspectives, including clinical health psychology, evolutionary psychology, developmental psychology and behavioral neuroscience. Then, discussion of models that are relevant to different pain types (i.e. acute or chronic) and developmental stages (i.e. infant or child/adolescent) will be explored.

Biopsychosocial Communication Model of Pain

The Biopsychosocial Communication Model of Pain (Hadjistavropoulos et al. 2011) outlines how pain takes place within a social context. Important features of this model include the impact of socialization on pain experiences and expression, as well as the inclusion of persons other than the individual experiencing pain, such as caregivers. The caregiver is particularly important in the context of pediatric pain given the dependence of children upon their parents for care. Although applicable to adults, this model has been mostly applied to children (and their caregiver). Four stages are differentiated within this model: Following a pain stimulus, a child is faced with an internal experience of pain (phase 1) that is then encoded into an expressive display of pain (e.g. facial pain behaviour), observable to others (e.g. parents) (phase 2). These expressive displays demand attention from others, which are then decoded (i.e. discriminated and interpreted) by the parent (phase 3), and may elicit emotional (e.g. distress) and behavioural responses (e.g. comforting) in the parent (phase 4) (see also Goubert et al. 2005). In turn, parents' responses impact on the child's experience and expression of pain (e.g. Racine et. al., 2016; Campbell et al. 2017).

The Biopsychosocial Communication Model of Pain has had a large influence on empirical work trying to elucidate the biopsychosocial influences on paediatric pain. It brings to the forefront the concept that the perception of pain is a social experience. It provides a heuristic framework that describes how the social context can impact both the expression and experience of pain. It is predicated on social influences having similar influences on both the person who is in pain, and the individual who is caregiving or supporting the person in pain, regardless of developmental stage. While acknowledging that the social context is critical in importance across the lifespan, other researchers have taken a more narrow focus within a certain developmental stage due

to the more prominent dyadic dependence that exists between parent figures and their children due to their immaturity. Below paediatric pain models will be discussed that focus on biopsychosocial models that focus on a stage or stages within childhood and also hone the focus specifically to either acute or chronic pain.

A Biopsychosocial Model of Infant Acute Pain: The Development of the Infant Acute Pain Responses Model- Revised (DIAPR-R)

The original DIAPR model (Pillai Riddell et al. 2013) was the first paediatric pain model that provided a framework for understanding the phenomenon of infant pain, specifically pain over the first year of life. It built upon key principles of the Socio-Communication Model of Pain (Craig and Pillai Riddell 2003) that posited the social context as an integral part of understanding the child in pain and the independent impact of these social contexts (such as families, schools and cultures) upon the child and the caregiver. However, a longitudinal program of research that focused on the infant and caregiver in an acute pain context over the first year of life (The Opportunities to Understand Childhood Hurt Cohort [OUCH Cohort], e.g. Pillai Riddell et al. 2011, Campbell et al., 2013, Din Osmun et al, 2014) allowed for novel insights that were not previously possible with cross-sectional data that did not use multivariate modelling techniques. These insights necessitated a new model that specifically accounted for the mechanisms elucidated during this unique development stage. Novel aspects of the original DIAPR model related to the need to explicitly draw attention to the different influences at play when trying to predict an infant's immediate behavioural pain reactivity versus trying to understand the infant's behavioural pain regulation or responses reflecting the return to homeostasis (Din Osmun et al., 2014; Lisi et al. 2013). Another novel mechanism based on initial analyses of the OUCH Cohort was that larger systems, such as culture, did not act directly on the infant's pain reactivity and regulation but actually acted indirectly on the infant through the caregiver (O'Neill et al. 2016). This new finding synergized well with developmental psychology's long held proposition that the infant is innately hardwired to signal a caregiver when distressed rather than trying to contextualize any distressing situation for themselves (Bowlby, 1969/1982). Thus, over the first year of life, the original DIAPR model sharpened the conceptualization of infant acute pain as having different stages (i.e. reactivity and regulation) that have different interrelationships with the factors influencing infant pain responses. Moreover, the DIAPR model postulated that during this early phase of the lifespan, larger systems (such as the family, medical institution, or one's culture) do not act directly on infant pain responding but do so via the caregiver.

The original OUCH cohort focused on examining psychosocial factors and infant and parent behavioural responding involved in the infant pain context. However, to forward our understanding of infants undergoing acutely painful procedures, it was necessary to broaden the focus beyond behaviours. The DIAPR-R expands the scope of the model to include pain-related behavioural responses, autonomic nervous system responding (e.g. heart rate) and the phenomenon of nociception and perception- an expansion made possible through collaboration with basic biological scientists. Synergizing the behavioural and psychosocial insights from the OUCH Cohort with the pioneering developmental neurobiological research by the Fitzgerald research group at University College London, a revised version of the model i.e. the DIAPR-R, has begun to take shape (See Figure 1).

- Insert Fig. 1 (DIAPR-R) about here -

Overview of the first revision of the DIAPR Model: The DIAPR-R Model

The model begins with the acutely noxious stimulus, such as a vaccination needle or a heel lance, which triggers an initial post-procedure sequence of events within the infant's peripheral and central nervous system (the first rectangle in the model). Occurring concurrently with nociception are the initial somatic behaviours and autonomic nervous system (ANS) physiology that define early reactivity (the initial milliseconds of the infant's pain-related responses that do not have to be centrally mediated; Verriostis et al., 2016). As the milliseconds pass after the initial noxious input the infant perceives the painful stimulus and is able to mount behaviours that are more centrally controlled which interact with the infant's ongoing autonomic nervous system reactivity (e.g. heart rate, cortisol) and pain-related behaviours. Once the peak pain-related reactivity has passed the infant's observable somatic behaviours and ANS physiology reflect the young child's return to baseline or measurable indicators of pain-related regulation. This acute pain responding sequence, right after the procedure, from nociception and perception to pain-related reactivity then pain-related regulation, is impacted by the caregiver context. Starting with the anticipation of a noxious stimulation in their child, it is hypothesized that a parent's pain schemas and stress physiology will become engaged as the caregiver begins to engage in a caregiving cycle (the oval to the far right of the model). The caregiving cycle relates to the ongoing processing by an adult (e.g. parent, nurse) of the infant's observable behaviours that involve their pain schemas, their own physiological responses to the infant's pain-related distress, their assessment of the infant's pain-related distress and their pain management behaviours. As in the original DIAPR model, the caregiving cycle is seen as the mechanism by which external systems such as culture or family norms (i.e. the triangle to the top) impacts infant pain responses.

At the bottom of the figure are important feedback loops that represent the dyadic nature of infant pain responses. This model purports that infant pain responding is dependent on the caregiving cycle. The initial pain-related reactivity happens only after the application of the acutely painful procedure (i.e. the first peak responses; peak distress most likely passes within 30 seconds of the termination of the painful procedure in healthy infants (Pillai Riddell et al., 2013) and is postulated to be determined more from the infant's pain thresholds and the noxious stimulus itself. Subsequent responding (i.e. after the first peak responses) is seen as more dependent on feedback loops with the caregiving cycle. Both the non-immediate pain responses and the caregiving cycle then continue to feedback on the perception of the pain. However, this feedback may potentially include nociception if the nature of the initial pain stimulus is ongoing (e.g. a chest tube insertion is a more prolonged acute medical procedure rather than a brief vaccination needle). In addition to acknowledging feedback loops occurring over the course of a single appointment, it is also important to recognize that these caregiver feedback loops also occur over appointments. This means that we should not just consider a painful vaccination response (either infant or caregiver) in isolation but recognize that they influence each other over many painful procedures or events over early life. Aspects of the caregiving cycle during infant

painful procedures are one of the most powerful predictors of preschooler vaccination distress and pain (Racine et al. 2016; Campbell et al., 2017).

Specific components of the DIAPR-R Model

Nociception-Perception Rectangle: For the purposes of this model, nociception is defined as the cascade of events from the peripheral nociceptor to the first afferent signals in the primary and secondary somatosensory cortex, while perception is defined as the more widespread cortical activation involved with making sense of the activation in the somatosensory cortex and involves areas such as the anterior and mid-cingulate cortex, insular cortex, amygdala, and regions of the prefrontal cortex. It is critical to recognize that, unlike other sensory modalities, cortical processing of noxious input reflects diffuse patterns of activation throughout the brain (Verriostis et al., 2016). These cortical processes are represented with one rectangle to denote that the cortical transition between nociception and perception has no clearly defined phases. For example, while work has elucidated a promising cortical indicator (i.e. the N3P3 wave form or the nociceptive event-related potential) to noxious stimuli (Slater et al., 2010) that is sensitive to contextual factors such as stress (Jones et al., 2017), it is still unclear if this cortical event represents nociception, perception, or both. The gradient colouring of the nociceptive side of the rectangle was purposefully matched to the initial part of the 'pain-related reactivity to pain-related regulation' rectangle. This matching of colouring gradient was to reflect that the infant's initial pain responding (i.e. the very first non-cortically mediated behavioural responses and physiological responses of the autonomic nervous system) are actually a part of nociception, which then blend into pain responses that are a result of cortical processing of the noxious stimulation (i.e. perception).

Pain-Related Reactivity to Pain-Related Regulation Rectangle: A number of aspects of this component have changed from the original DIAPR model. First, the combination of reactivity and regulation within the same rectangle reflects the idea that reactivity and regulation, while operationalized as distinct, are aspects of the same pain response and there are no clear delineations that denote that reactivity has ended and regulation has begun. It could be argued that ultimately, the minute the noxious stimuli is removed the infant is moving back towards homeostasis. Second, the dark shading within this left most side of the box reflects the temporal connection of initial behaviour and physiology that are part of initial nociception (Verriostis et al. 2016). For example, there are initial reflex arcs to an acutely painful stimulus (both behaviour and autonomic nervous system physiology) that can be spinally mediated (i.e. a part of nociception rather than a consequence of nociception), in addition to the more traditional linear sequence from nociception to perception to reactivity to regulation. Also, it must be acknowledged that at times there may not be a behavioural, cortical, and/or physiological response to a painful stiumulation. It is an important area to pursue what non-responding means particularly for caregivers wanting to prevent longer term implications of pain exposure.

The Caregiving Cycle Oval: This piece of the model represents the ongoing evaluative and responsive cycle that caregivers go through when interacting with a child in pain. Rather than seeing it as a linear process, the circular shape reflects how this process feeds back onto itself both in how a caregiver thinks (i.e. pain schemas and assessments)

and responds (pain management and ANS physiology). A unique feature that is more prominent in young children, particularly infants, is that a caregiver's ANS physiology could have a direct impact on the infant pain responses if the infant is being held skin to skin on a caregiver's bare chest. Based on research on mother-infant attunement (e.g. Feldman et al. 2011), we speculate that when an infant's positioning is in a caregiver's arms, chest to chest, caregiver heart rate can be heard and/or felt and the speed of heartbeat would communicate either calming or distress messaging to the infant.

The above DIAPR-R model delineates a framework that focuses on a specific stage within childhood where the dependency of child on caregiver is at its greatest. While the processing of acute pain is postulated over time, both over an epoch surrounding a painful medical procedure within infancy and over infancy itself, this model does not address the type of pain that persists. The next models postulate integrative conceptual models for understanding paediatric chronic pain and disability in older children.

Biopsychosocial Models of Paediatric Chronic Pain

Different than the acute procedural pain of the DIAPR-R model that is iatrogenically caused from outside the individual, the persistence of pain is predicated on pathological biological processes. Acute nociceptive pain serves to warn individuals that there is harm and attention must be paid to the bodily area signalling distress. Acute pain impedes movement and grabs attention away from current activities to signal the individual to take action. Within the much more complicated situation where pain persists, often the definition of 'chronic pain' is predicated on the fact that the pain serves no apparent function and continues beyond what would be expected for normative healing time. This definition can include pain that is persistent and ongoing versus recurrent and episodic due to pathology within the nervous system. Simplistic dichotomies that separate the biological from the psychosocial are not only incorrect but actually are detrimental to the patient, particularly children (American Pain Society Task Force on Pediatric Chronic Pain Management; accessed March 20, 2018). Because humans change most significantly over the course of childhood, formulations of pathological nervous system processes must be contextualized with physical, psychological, and social development.

<u>Conceptual model for Understanding Paediatric Chronic Pain and Disability</u>

Palermo and colleagues (Palermo 2012, Palermo et al., 2014) discuss the importance of understanding the child's developmental stage when understanding the interplay of social, psychological, and biological dimensions of a child's experience. It is explicitly acknowledged that familial and parent factors exert different influences from infancy to adolescence. As shown in Figure 2, there are four major aspects of the model. The biological substrate of the model acknowledges that aspects of development (either body or brain) will impact pain experience and expression. Pubertal development and sex play different roles in paediatric chronic pain in older versus younger children. Providing a context to the biology of pain, psychological variables, such as mood, anxiety, coping and catastrophizing are also proposed as critical components to understanding chronic pain, due to a strong convergent evidence base. Both the child's psychology and biology are seen to interact in the larger social context. Thus, a family's composition, a child's school or peer context, or their socioeconomic status all add

important nuance to understanding the child or adolescent in chronic pain. An interesting component not commonly made explicit in models of paediatric pain are health habits. For example, aspects of a child's behaviour such as sleep schedule, smoking, exercise and use of prescription or illicit drugs are postulated to play a role in moderating pain and pain-related disability across the three primary systems (biological, psychological, and social). The complexity of the interplay between the three primary systems is demonstrated through bidirectional arrows. Moreover, health habits develop and change based on this interplay.

Rather than focus on specific variables, this model comprehensively takes a larger conceptual view to provide a framework for understanding chronic pain in children and adolescents. However, because of the 'big picture' view, specific mechanistic hypotheses of how different systems act on each other and how they change over time are not readily extracted from the model. These mechanisms are critical to treatment. Current directions in paediatric chronic pain models come from a biopsychosocial approach to treating pain, but focus more specifically on psychosocial mechanisms that could be empirically tested through statistically modelling relationships posited between key constructs. The next sections describe recent models postulated in the literature that speculate specific psychosocial mechanisms (i.e. learning and cognitive-behavioural mechanisms) within the biopsychosocial context of chronic pain.

- Insert Fig. 2 (Tonya Palermo's 'Conceptual model for understanding paediatric chronic pain model") about here -

Interpersonal Fear Avoidance Model (IFAM)

Pain is an experience that drives learning. Every day humans learn about the circumstances of pain: the antecedents that predict and cause pain (classical conditioning), and consequences that maintain (chronic) pain (operant conditioning). Specifically, individuals learn to fear impending pain and which actions should be undertaken to minimize pain and to avoid it on future occasions (Goubert et al. 2004). Fordyce was one of the first to systematically apply learning principles to chronic pain (Main et al. 2015). Learning also continues to play a role in more recent biopsychosocial accounts of chronic pain. For instance, the principles of classical and operant conditioning are of paramount importance in fear-avoidance models, which postulate the centrality of fear and avoidance in the development of chronic pain problems in adults (Vlaeyen & Linton 2012) and children (Asmundson et al., 2012; Simons & Kaczynski 2012; Goubert & Simons, 2013). A key determinant of adverse child outcomes may be a child's prioritized focus upon pain relief resulting in avoidance of daily activities (e.g. school, hobbies), motivated by fearful and catastrophic thoughts about pain. Prolonged avoidance of daily activities may result in long-term disability, child depression, and delays in the normal child's development. Indeed, prioritized pursuit of pain control goals may hinder the pursuit of developmentally appropriate goals, such as the achievement of new academic and social skills. Children who endorse high levels of worrisome thoughts about pain (i.e. catastrophize) may be likely to become entrapped into a vicious cycle of pain, fear, and prolonged disability (Asmundson et al., 2012; Simons & Kaczynski 2012).

Child pain takes place in a social context, of which parents are most influential social agents. In 2013, an interpersonal account of the Fear-Avoidance Model was developed, the Interpersonal Fear-Avoidance Model (IFAM, Goubert & Simons 2013), highlighting the central role of parents' cognitions, emotions, and behaviours in impacting children's pain experiences and functioning (see Figure 3). A key parental characteristic is the extent to which the parent excessively worries – or catastrophizes – about the child's pain (Goubert et al. 2006). Parents who perceive their child's pain as highly threatening often experience high distress, and, accordingly, feel motivated to engage in behaviours aimed at the reduction or avoidance of pain in their child (so-called "protective" or "solicitous" behaviours, such as keeping the child home from school), at the expense of other important domains (e.g. school performance) in the child's life. Via operant conditioning principles, parental protective behaviours can reinforce children's avoidance behaviours, which can, over time, result in higher levels of disability and even depression. More protective behaviours from parents are associated with higher child disability (Peterson & Palermo 2004; Simons et al. 2008). Furthermore, higher parental catastrophizing about their child's pain is related to higher parental distress (Goubert et al. 2006; Caes et al. 2011), higher child disability and lower school attendance (Goubert et al. 2006), and a higher tendency to restrict their child's pain-inducing activity (Caes et al. 2011). When examining parent catastrophizing and protective parent behaviours together, protective behaviours mediated the relationship between parent catastrophizing and child school functioning (Logan et al. 2012) and partially mediated the relationship between catastrophizing and functional disability (Sieberg et al. 2011). Using the recently developed Parent Fear of Pain Questionnaire (PFOPQ; Simons et al., 2015), parent protective and avoidance behavior contributed directly and indirectly to child avoidance while parent fear and catastrophizing contributed indirectly to child avoidance through parent behavior and child fear and catastrophizing, in turn, influencing child functional disability levels. Parental pain-related fears have also been related to more child healthcare utilization in addition to higher levels of child functional disability (Simons et al. 2011). The Interpersonal Fear Avoidance Model delineates negative responses for parents. When the child's pain becomes chronic parents may become continuously focused upon the goal of alleviating their child's pain, which might interfere with their own personal goals (e.g. work performance). In addition, parents may experience frustration, feelings of incompetence, and eventually depressive feelings, which might, in turn, impact on the child (see Figure 3).

Parental beliefs about pain and parental behaviours may not only influence children's pain and disability through the parents' (protective) behaviours but also by means of *observational learning processes*. Observational learning or modelling was first outlined in the Social Learning Theory by Bandura (1977) who defined observational learning as "changes in patterns of behavior that are a consequence of observing the behavior of others". Through observation of another's (e.g., parent's) behavior in a particular situation, a child acquires information about that situation and about the consequences of specific actions in that situation. As shown in Figure 3, pain-related fears and catastrophizing thoughts in parents may transfer to their child, fueling his/her fears and worries. How parents perceive and cope with pain may impact children's beliefs and behavioural repertoire (Goubert et al. 2011). For example, a child who observes her mother displaying fear and avoidance reactions to lifting a heavy shopping bag, may adjust her appreciation of that particular situation ("lifting activities are dangerous") and the behavioral consequences ("not engaging in lifting that is back-stressing avoids

pain experiences"). Research about observational learning as sources of beliefs about pain and its treatment, pain-related fears and behavioral responding is still limited (Goubert et al. 2011) even considering early work demonstrating a powerful impact of models who were (in)tolerant of pain was undertaken by Craig and colleagues several decades ago (for an overview, see Hermann, 2007).

An experimental study in schoolchildren and their mother (Goodman & McGrath 2003) demonstrated that children observing their mothers' reactions during painful exposure of the hand in cold water subsequently displayed lower pain thresholds when their mother had voluntarily exaggerated her pain. Furthermore, children displayed reduced facial displays of pain when the mother had voluntarily suppressed her reaction. In a recent study (Stone, Brueyl, Smith, Garber & Walker, 2017) using a diary approach in adolescents with functional abdominal pain, higher levels of parent pain behaviors observed by adolescents had a stronger relation to adolescents' pain severity and impairment than parental protective behaviours, but only when the parent had chronic pain. These results were corroborated by Stone and Walker (2017), who demonstrated that adolescents with functional abdominal pain who observed more frequent pain behaviors in their parents report higher levels of pain-related interference. These findings provide indications for the importance of observational learning processes in the intergenerational transmission of pain.

- Insert Figure 3 Interpersonal Fear-Avoidance Model about here -

In addition to the overt behaviour captured in the Interpersonal Fear-Avoidance Model, Goubert, Simons and colleagues have recently put forth a theoretical argument that paediatric chronic pain can potentially produce a number of stressors impacting the parent-child interaction that can result in pertubations in *parent* brain processes that manifest as alterations in physiology, behaviour, and emotional state (Simons, Goubert, Vervoort, & Borsook, 2016). A central concept in the potentially brain modulating impact of child pain on the parent brain is empathy (Goubert et al., 2005). Empathy in the context of pain is defined as *"a sense of knowing the experience of another person with cognitive, affective and behavioural components"* (Goubert et al., 2005; Goubert et al., 2013). Empathizing with another involves implicit and explicit processing of another's emotional experiences and also the production of a parallel emotion state in oneself. Current evidence ties heightened distress and empathic responding when faced with another in pain (Lamm et al., 2016). Several studies have also identified neural correlates of empathy (Shamay-Tsoory, 2011), such as the broader salience network (inclusive of cingulate, anterior insula, and medial prefrontal cortex, cerebellum, pulvinar) (Borsook et al., 2013a). Empathy in the context of pain is a core process by which the observation of pain may impact others and is an essential process to understanding the plight of a parent whose child is suffering.

The topography of parent empathic behaviour in the context of a child's pain provides important keys to its neurobiological roots. High emotional contagion is a front-runner for explaining empathic distress and maladaptive responses (e.g., miscarried helping behaviors) in parents. As parents often are a child's primary care taker, their level of adaptation to stress is an important consideration. Resilient parents may provide heartfelt, calm emotional support during a child's distress. Moreover, positive affect and dispositional optimism can provide enormous beneficial responses to treatments. As an

example, examination of interactions between parents and children with cancer, parental adaptive affective empathic responses (empathic concern/other-oriented minus state anxiety/self-oriented) predicted child positive disposition and less observed pain/distress during cancer treatment (Harper et al., 2012).

Conversely, empathic distress is associated with increased pain in children (Penner et al., 2008) and a parent's behavioural response (likely aimed at regulating their own heightened distress) may inadvertently contribute to the maintenance of their child's pain complaints (Dolgin and Phipps, 1989). High levels of emotional contagion likely drive the empathetic distress exhibited in parents and is best exemplified in the overt cognitive and behavioural elements captured in the Interpersonal Fear Avoidance Model (e.g., pain catastrophzing, fear, protective behaviour)(Caes et al., 2012)(Lynch-Jordan et al., 2013)(Sieberg et al., 2011)(Logan et al., 2012). Although it seems paradoxical that protective parenting behaviour can lead to negative outcomes, this can be understood in the context of the underlying emotional/empathic state that motivates the behavioural response. In this case, parents' drive to decrease their (own) distress dominates, with fewer cognitive resources to be attuned to the needs of the other (child) independent of their own level of distress (Caes et al., 2011; Vervoort & Trost, 2017).

While the Interpersonal Fear Avoidance Model predominantly focuses upon risk factors for maladaptive child functioning, recent efforts have also focused on processes and mechanisms that optimize the quality of life in families of a child experiencing chronic pain. As outlined by the Ecological Resilience – Risk Model below, both risk factors and resilience mechanisms should be considered when trying to understand and improve children's pain experiences and pain-related functioning.

The Ecological Resilience – Risk Model (ERRM)

A growing body of research on paediatric chronic illness demonstrates that many family units demonstrate substantial flexibility and resiliency in the face of ongoing interference due to chronic illness. For example, in a large-scale (N = 10,650) epidemiological study in Flemish young people (age range: 10-21 years; M_{age}=14.33 years), 19.1% reported experiencing high levels of pain accompanied by low levels of disability, thereby reflecting resilience despite being faced with chronic pain (Vervoort et al. 2014).

Resilience has been defined as "a dynamic and multi-systemic progression that allows the individual to respond effectively when faced with risk or adversity (e.g., chronic pain)" (Cousins, Kalapurakkel, et al. 2015). Importantly, the ERRM acknowledges that resilience originates within the individual, but can be enhanced through factors in the individual's social environment. The ERRM was originally derived from the adult chronic pain Risk-Resilience Model (Sturgeon & Zautra 2013), wherein resilience and vulnerability are two independent but related constructs that determine an individual's pain-related trajectory. Within the concept of resilience, it is important to distinguish between resilience 'resources', 'mechanisms' and 'outcomes' (see also Goubert & Trompetter 2017). Resilience resources are stable characteristics or traits (e.g., optimism and hope), while mechanisms are characterized as dynamic and modifiable processes (e.g., positive affect and positive relations) of a person and his/her social context. Resilience resources promote resilience mechanisms but may also minimize the

impact of vulnerability factors and mechanisms on individuals' functioning. These resilience and vulnerability pathways determine the resilience outcomes, which consist of three distinct components: 1) sustained engagement in highly valued activities, 2) recovery from stressful experiences such as pain flares, and 3) personal growth or benefit-finding (Sturgeon & Zautra 2013). However, most research to date has only focused on negative outcomes such as disability and distress. A resilience framework clarifies how considering and measuring both maladaptive pain-related (negative) outcomes and adaptive (positive) outcomes (e.g., engagement in values-based activities, psychological well-being, vitality, contribution to society) are important for our understanding of functioning well with persistent pain (Goubert & Trompetter 2017).

The Ecological Resilience-Risk Model (ERRM; Cousins, Kalapurakkel, et al. 2015) represents an adaptation of the adult model to reflect childhood pain experiences. Specifically, despite the dearth of research addressing the social context as a source of resilience, the resilience resources and mechanisms available in the child's social environment play a prominent role within the ERRM. The resilience and vulnerability pathways are proposed to occur within the individual and his/her social environment (including family, peers, school environment and culture), with a bidirectional relationship between the child's individual and social pathways determining the outcomes of the child in pain (see Figure 4).

Despite the strong theoretical underpinnings of the ERRM, many of the pathways have yet to be empirically examined. Preliminary findings do provide evidence for the role of resilience resources such as optimism, mindfulness, positive peer relations, teacher support, and supportive parent and family functioning in improving outcomes (e.g., increased quality of life and pain tolerance; reduced pain intensity and school absenteeism) for adolescents with chronic pain and their family (Cousins, Cohen, et al. 2015; Palermo et al. 2014; Petter et al. 2013; Vervoort et al. 2014). For the child with paediatric chronic pain, various research efforts (e.g., explorative, instrument development and intervention studies) point to the beneficial impact of child psychological flexibility, child acceptance of pain, child self-efficacy, and parental psychological flexibility on emotional and functional disability and improved school functioning (Carpino et al. 2014; Kalapurakkel et al. 2015; Wallace et al. 2015; Weiss et al. 2013; Beeckman et al., 2018).

Considerable research is needed to examine resilience mechanisms in paediatric pain such as the role of positive affect, psychological flexibility, committed action, parent modeling of active coping and promotion of activity engagement, benefit finding, and self-regulation (Cousins, Kalapurakkel, et al. 2015; Goubert & Trompetter 2017). Focusing on the role of resilience mechanisms, and how they interact with vulnerability factors in the context of paediatric chronic pain is of critical importance to optimize clinical interventions. Specifically, resilience resources and mechanisms may be easier to influence and reinforce than vulnerability factors and therefore may play a key role in clinical practice (Hilliard et al. 2012; Goubert & Trompetter, 2017).

- Insert Figure 4 (Ecological Resilience-Risk Model; ERRM) about here -

Clinical implications

Approaching clinical problems with solutions derived from solid theory has led to breakthroughs across medicine and science for many years. Making progress in understanding and effectively treating pain in childhood is no different. As the field progresses, so does our need for theoretical understanding. Across both acute and chronic pain, social communication is a key element that predicts the outcome (positive or negative). Thus, clinical approaches in the acute and chronic pain context that incorporate the parent directly likely yield the greatest promise for success.

The DIAPR-R model provides an innovative approach to conceptualizing an infant's acute pain response. Bolstered by collaboration between basic behavioural and basic biological science laboratories, the DIAPR-R model reflects a large body of work that examines how the caregiver shapes the initial response and the regulation of pain over the first years of life with an integrated discussion of biology, behaviour, cognition, affect and social components. An important clinical implication of this work underscores the power of parents. Clinicians and scientists need to learn more effective ways to train parents to make a clinically meaningful difference in managing and preventing their infant's pain-related distress. While traditional approaches have focused on sensitive behaviours, recent work suggests that teaching parents to avoid empirically-supported distress-enhancing behaviours may be much more powerful (Gennis et al., in press; Badovinac et al., in press).

For chronic pain in childhood, recent models place the social context (parents, family, peers) as central tenets in understanding its persistence or amelioration. These models provide several points of intervention that begin at the point of evaluation. Assessing (and potentially shifting) the goals of children and parents when facing chronic pain is critical. When the unsuccessful search for a solution for the pain problem dominates family life at the cost of other important life goals, families may need to give up the primary goal of pain relief. This idea has been put forward in concepts such as acceptance, derived from Acceptance and Commitment Therapy (ACT), which has been defined as halting the dominant search for a definitive cure for pain and re-orienting one's attention toward positive everyday activities and other rewarding aspects of life (McCracken & Eccleston, 2003). Although most research on acceptance-based strategies has taken place in the context of adult pain (Veehof et al., 2016), this approach has been successful in adolescents (Wicksell et al., 2007, 2009). These researchers found that enhancing psychological flexibility (Wicksell et al., 2011) is a key mechanism of change predicting reductions in disability following treatment. Applying mindfulness and acceptance-based approaches are likely also warranted for parents who struggle with empathic distress. Individuals who are prone to engage in empathic distress, avoid negative thoughts, feelings, memories, physical sensations, and other internal experience in the short-term (for the momentary relief) – even when doing so can create harm in the long-run (Hayes, Strosahl, & Wilson, 2015), due to the power of negative reinforcement. Importantly, it is not the negative thoughts, emotions, or sensations that are problematic, but how one responds that can cause life impairments. Thus, these resilient-based approaches are likely as important to be implemented directly with parents. A recent pilot study by Wallace et al. (2016) provided preliminary support for the efficacy of an intervention promoting psychological flexibility in parents of

adolescents with chronic pain; results showed that protective parenting responses decreased during follow-up as well as adolescents' pain interference. These findings suggest that resilience-based approaches such as Acceptance and Commitment Therapy may be important to enhance adolescent functioning and to address parents' distress and maladaptive parenting behaviours (e.g., overprotective behaviours).

Conclusion

In this chapter, we outlined how a child's pain experience, behaviour and pain-related functioning can be impacted by biological (neurological), psychosocial and social factors. Several theoretical models are discussed referring to acute or chronic pain in childhood. As children are dependent upon others for care, the social context is important in determining children's pain experiences and functioning. Parents, as direct caregivers, play an important role, in children's acute and chronic pain experiences. This chapter also emphasizes that both risk and resilience mechanisms should be taken into account when considering adaptive functioning in children. Future research should examine the resilience mechanisms, both within the child as within the social context, that may help children to cope well with pain as well as to keep on functioning well in the face of chronic pain. Knowledge on crucial resilience resources and mechanisms may further inform clinical interventions to prevent child pain-related disability and promote sustained child engagement in values-based activities. Given the crucial role of parents, it will also be important to examine how parents can be a social source of resilience for their child and how parents can be included in clinical interventions to promote child resilient functioning.

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Perspective Box

Discussion questions: Across all the evidence presented, parents have been shown to be influential in shaping or modifying their child's pain responses.

1. What are the potential biological mechanisms that could explain how a parental social context impacts pain modulation?
2. Should paediatric clinicians routinely screen and find supports to address parent mental health support as a key factor in supporting child chronic pain?
3. When a parent has chronic pain, what type of components could be added to a paediatric chronic pain intervention to work with both parents and children to increase resilience in both members of the dyad?

4. If a parent has a phobia or high anxiety around a child's medical procedure, what types of psychological interventions could be developed to support the parent in supporting their child?

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