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Article in *Pain Management* · September 2012

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Pain is not over when the needle ends: a review and preliminary model of acute pain memory development in childhood

Melanie Noel^{*1,2}, Christine T Chambers¹⁻⁴, Mark Petter^{1,2}, Patrick J McGrath¹⁻⁵, Raymond M Klein¹ & Sherry H Stewart^{1,4,6}



Practice Points

- The field of pediatric pain has come to appreciate the importance of children's early pain memories in influencing their subsequent pain experiences.
- This review synthesizes selected studies that made a significant impact on this field of inquiry, with particular emphasis on recent clinical and experimental research examining children's explicit autobiographical memories for acute pain.
- Research is beginning to enhance the precision with which children at risk for developing negatively estimated pain memories can be identified, in light of the adverse influence that these memories can have on children's subsequent pain experience.
- Although there is a dearth of research examining the effectiveness of memory reframing interventions, these treatments hold promise for reducing the adverse impact of inadequately managed pain.
- With the development of new assessment tools and the pediatric fear-avoidance model of chronic pain, future research should examine the influence of child and parent fear-avoidance variables in the development of children's memories for pain.
- A preliminary empirically and theoretically derived model of children's acute-pain memory development is proposed, which outlines the factors and relationships implicated in the process by which children's pain memories develop, are reframed and influence the pain experience over time.

SUMMARY Over the past several decades, the field of pediatric pain has made impressive advances in our understanding of the pain experience of the developing child, as well as the devastating impact of inadequately managed pain early in life. It is now well recognized that, from infancy, children are capable of developing implicit memories of pain that can influence their subsequent reactions to pain. The present review provides a synthesis of selected studies that made a significant impact on this field of inquiry, with particular emphasis on recent clinical and laboratory-based experimental research

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examining children's explicit autobiographical memories for acute pain. Research has begun to move towards improving the precision with which children at risk for developing negatively estimated pain memories can be identified, given the adverse influence these memories can have on subsequent pain experiences. As such, several fear- and anxiety-related child and parent variables implicated in this process are discussed, and avenues for future research and clinical intervention are identified throughout. Finally, a preliminary empirically and theoretically derived model of acute pain memory development in childhood is presented to parsimoniously summarize the evidence accumulated to date and guide future investigation in this area.

40 years ago, it was widely believed that infants could not feel pain [1], which led to inadequate treatment and needless suffering [2]. Prior to the 1980s, infants were also believed to be incapable of encoding, storing and retrieving memories of past autobiographical events [3]. Recognition of the importance of children's memories for pain was largely inspired by landmark studies that were published prior to the turn of the millennium. The seminal research by Taddio and colleagues provided evidence of the adverse impact of poorly managed pain in the first days of life on subsequent pain experienced at 4 and 6 months [4]. Infants who were circumcised without the use of topical local anesthetic, as compared with infants who were uncircumcised, displayed a greater pain response and cried longer at a subsequent routine immunization. Furthermore, the infants circumcised with placebo were observed to experience a greater increase in pain during the subsequent immunization than infants circumcised with topical local anesthetic. These researchers subsequently demonstrated that infants of diabetic mothers who were exposed to repeated heel lances in the first 2–3 days of life, as compared with infants who were not exposed to repeated painful procedures, exhibited a greater pain response prior to (i.e., during skin preparation and cleansing) and during a subsequent venipuncture [5]. These studies dramatically demonstrated how inadequately managed pain in the first days of life could lead to sensitization to later pain experiences. This research also raised the possibility that these infants learned to anticipate pain during a subsequent procedure and developed some form of implicit pain memory that influenced their distress during subsequent pain [6]. This early work provided critical evidence for the powerful role of children's early memories for pain in their subsequent pain experience and established the importance of this area in the field of pediatric pain.

Indeed, children's memories for pain have important implications for pain assessment, treatment and health across the lifespan [6,7]. Many of the tools used to assess pain rely on the child's retrospective account of their psychological and physical experience of pain (e.g., comparison between current and remembered pain experience) and memory for pain is often used to infer the effectiveness of current interventions. Additionally, memories for pain may play an important role in the transition of pain from an acute to chronic state [8,10], through operant and respondent learning processes as well as altered processing within the CNS [8]. Moreover, early memories for pain can have important long-term consequences for subsequent health behaviors and pain perception. Retrospective research suggests that early pain memories influence fear and avoidance of medical care in adulthood [9]. Furthermore, among both clinical and healthy samples, children who develop pain memories that are negatively estimated (i.e., recalled pain is higher than initial pain report) are at risk for experiencing increases in distress and pain over time [10,11]. As such, children's memories for pain are as important to their subsequent health behaviors as their actual experience of pain itself.

The purpose of this review is to offer a contemporary perspective on recent issues in the field by providing a synthesis of selected studies that have made significant contributions to our understanding of children's explicit memories for acute pain, with particular emphasis on recent clinical and laboratory-based experimental research. In addition, a novel preliminary theoretical model of children's acute pain memory development, inspired by this research, is presented to stimulate future research in this area. Finally, avenues for clinical intervention are highlighted throughout. Given that this review paper is not intended to be a systematic review or meta-analysis, a formal search strategy was not applied.

Children's pain memories: the state-of-the-science

Pain memories are – not unlike the pain experience [12] – subjective and multidimensional, consisting of sensory (e.g., pain intensity), affective (e.g., fear) and contextual (e.g., people, place and time) aspects [7]. Children's memories for pain are constructive and reconstructive, which makes them susceptible to distortion over time. The manner in which memories are framed is influenced by a host of factors including: age [13]; distress [10]; pain intensity [14]; trait anxiety [15]; negative affectivity [16]; parent–child discourse about the event following exposure [17]; duration of the interim between pain experience and memory assessment [18,19]; and state anxiety at the time of memory elicitation [20]. As a result, empirical investigation in this area is methodologically complex. Nevertheless, given the importance of children's pain memories in shaping their subsequent pain experiences, garnering understanding of the processes involved in children's pain memory development is of critical importance.

Previous reviews on children's memories for pain

There is a substantial body of literature on the development of children's autobiographical memories for stressful and traumatic events (for reviews, see [21,22]); however, specific research on children's memories for pain is relatively limited. To date, two reviews on the topic have been conducted. The first, by Ornstein and colleagues, provided an overview of research that was primarily conducted with children in medical procedure contexts [7]. The authors provided an information-processing framework outlining the various stages of memory (encoding, storage and retrieval), informed by literature on children's autobiographical memory development within which the acquisition, retention and distortion of information about pain experiences can be organized and understood. Despite the importance of this initial review, the majority of studies reviewed assessed children's memory for contextual details as opposed to aspects of the pain itself. As such, it was unclear whether the same principles underlying children's contextual memory also applied to memory for somatosensory and affective aspects of pain. The second review, by von Baeyer and colleagues, provided an overview of developments in the field since the time of the original review, emphasized the

consequences of children's pain memories for subsequent pain and healthcare behaviors, and discussed individual differences as well as situational and methodological influences in children's recall [6]. Importantly, this review highlighted the individual variability in children's pain memories and resulting health behaviors as well as potential intervention targets that could prevent the deleterious consequences of negatively estimated pain memories.

Fragility of pain memories

Children's autobiographical memory – the type of explicit memory of an event from one's life that is tied to a particular place and time (e.g., a painful medical procedure) – has been described as remarkably robust yet significantly fragile [23,24]. Similar to memory for stressful events, children have generally been found capable of accurately recalling previous painful experiences; indeed, children as young as 3 years of age are fairly accurate at recalling contextual aspects of painful medical procedures, especially in the absence of specific or leading questions [25,26]. Similarly, among both healthy and clinical samples of children undergoing experimental and medically induced pain, children's pain memories have been found to be accurate after short (e.g., 1 week) and long (e.g., 1 year) delays [27–29].

Nevertheless, the fragility of pain memories is rooted in the fact that memory can become distorted over time [10,14,15,30]. Bruck and colleagues conducted an investigation that provided the first and perhaps most compelling demonstration of the reconstructive nature of children's pain memories [31]. They examined children's memories for contextual details of, and pain experienced during, an immunization as well as the effect of providing children with different types of information following the procedure on their subsequent recall. Following immunization, children were randomly assigned to receive either pain-affirming (e.g., 'the shot hurt'), pain-denying (e.g., 'the shot did not hurt'), or neutral (e.g., 'the shot is over') feedback. Children's recalled pain and observer-reported distress ratings (i.e., based on facial features, verbalizations and degree of crying) did not differ 1 week later; however, approximately 1 year later (range: 4–18 months) the researchers conducted follow-up home visits on three separate occasions to provide additional pain-denying or neutral feedback and misleading or nonmisleading (e.g., falsely stating

that the pediatrician read a story to the child) information about the individuals involved in the children's care. At a fourth and final visit, children who received pain-denying feedback remembered crying less and experiencing less pain than children who received neutral feedback. Furthermore, children who received misleading information made more false allegations regarding the individuals involved in their care (e.g., reported that the research assistant gave them the vaccination) than children who did not receive this misleading information. Interestingly, those children who exhibited greater distress during the immunization were found to be more susceptible to suggestibility 4–18 months later. Together, the findings demonstrated the malleability of children's pain memories and the impact that discourse surrounding the experience following the event can have on subsequent recall.

Memory distortion & subsequent pain experience

Once children's pain memories become distorted, they can have important implications for distress experienced during subsequent pain experiences. Chen and colleagues examined this possibility among children diagnosed with leukemia who were required to repeatedly undergo lumbar punctures spaced 1 week apart as part of their treatment protocol [10]. Although children's pain memories were generally accurate, a subset of children later developed exaggerated memories of the negative details of the lumbar puncture (described in more detail below). Furthermore, children who developed more negatively estimated, versus accurate or positively estimated, memories of pain and anxiety exhibited greater increases in behavioral distress (i.e., observer-rated behaviors that are indicative of anxiety and/or pain such as crying, screaming and verbalizations of anxiety), and reported more pain over time. This was a robust finding that persisted even after controlling for age, initial distress and number of previous lumbar punctures. This research highlighted the importance of memory distortion for subsequent distress and identified children who are most at risk for developing maladaptive responses to pain versus those who may be buffered from such outcomes.

A recent investigation by Noel and colleagues extended this research among healthy children undergoing a novel experimental pain task [11].

Children completed the cold pressor task on two laboratory visits spaced 1 month apart. At 2 weeks following the initial exposure, children's memories for the pain task and expectancies about future pain were elicited. Similar to healthy adults [16], children's memories of pain intensity were a better predictor of subsequent reporting of pain intensity than was their actual initial experience of pain; in fact, children's memories fully mediated the relationship between pain reporting at the initial and the subsequent pain experience. Similar to children with chronic illness [10], differences in children's memory style also influenced subsequent pain reporting. Children who developed negatively estimated, versus accurate or positively estimated, memories of pain intensity and pain-related fear developed more negative expectations of future pain and showed greater increases in pain ratings over time.

Individual vulnerability & protective factors

Given the potential malleability of children's pain memories and the importance of negative distortion for subsequent pain and distress, research has moved towards identifying children who are most at risk for developing negatively estimated pain memories. Although the relationship between stress and children's memories for autobiographical events is controversial and marked by inconsistencies across studies [13], in the context of pain there is a clear link between children's level of pain and distress experienced during a painful event, and the subsequent framing of their memories. Across a range of medical procedures and among both clinical and healthy samples, it has been demonstrated that children who exhibit greater behavioral distress and report higher levels of pain, tend to develop negatively estimated pain memories [10,14]. Chen and colleagues examined pain memories of children between the ages of 3 and 18 years who were diagnosed with cancer and who were required to repeatedly undergo lumbar punctures as part of their treatment protocol [10]. Higher distress at the initial lumbar punctures was associated with more negatively estimated pain memories, even when controlling for number of previous lumbar punctures.

To ensure the generalizability of these findings, Noel and colleagues examined the relationship between venipuncture pain experienced during routine blood draws and memories for

the somatosensory and affective aspects of the pain experience [14]. Consistent with previous research [10], children who reported higher levels of pain intensity during venipuncture later developed negatively estimated memories of anxiety. Similarly, children undergoing hepatitis vaccinations who received standard care (i.e., no pain management) developed more negatively estimated memories of pain intensity compared with children who received pharmacological (e.g., topical anesthetic) and nonpharmacological (e.g., distraction) interventions. These children also developed less accurate memories of anxiety than children who received pharmacological intervention [30]. Furthermore, children undergoing dental procedures who had higher levels of trait anxiety tended to recall more pain after a delay, suggesting that highly trait anxious children may have developed negatively estimated pain memories [15].

Anxiety & children's pain memories

In light of theoretical [32] and empirical [15] support for the role of anxiety in the development of memory biases for threat and pain, Noel and colleagues recently examined the causal impact of state anxiety, and the influence of anxiety-related variables, on the development of healthy children's memories for a novel pain experience [33]. Children were randomly assigned to complete either a laboratory state anxiety induction task (i.e., anticipation of giving a speech in front of judges and completing a difficult math task) or a control task (i.e., anticipation of watching a nature video) before completing the cold pressor task. Children also completed measures of anxiety-related variables (state/trait anxiety and anxiety sensitivity) and provided pain ratings immediately following the pain task and again 2 weeks later based on their memories. Results did not reveal memory differences between children in the state anxiety induction group and those in the control group; however, irrespective of group assignment, state anxiety emerged as a unique predictor of children's memories of pain intensity and pain-related fear, over and above sex, stable anxiety-related variables, and initial pain reporting. Moreover, anxiety sensitivity and trait anxiety significantly predicted children's memories of the fearful aspect of the pain experience. These predictive models had substantial explanatory power accounting for 52 and 35% of the variance in recalled pain intensity and pain-related fear, respectively.

This research extends findings yielded among healthy adults to earlier developmental periods [34] and further illustrates the importance of both state anxiety and trait-level anxiety variables in influencing the development of children's pain memories.

Memory reframing interventions

Given the powerful influence of pain memories on subsequent pain experience, intervention efforts should extend beyond the immediate pain context; however, very few studies have examined the effectiveness of memory reframing interventions to date. Chen and colleagues examined the influence of a brief memory reframing intervention on subsequent distress during repeated lumbar punctures among children diagnosed with leukemia [35]. Children in the treatment group's memories were elicited through a memory interview designed to assess biases in children's recall of threatening aspects of the lumbar puncture. Subsequently, a therapist who observed the procedure used cognitive-behavioral strategies to reframe the memory based on objective information yielded during the procedure. Specifically, therapists assisted children in re-evaluating their reactions by reinforcing their beliefs about their abilities to use coping strategies (e.g., increasing their perceived self-efficacy), appraising their responses to the procedure in a more realistic manner and increasing the accuracy of their recall. In this way, the intervention directly targeted and aimed to reduce the catastrophic and negatively estimated aspects of children's recall, and aimed to increase children's perceptions of the effectiveness of their coping abilities. Compared with children in the control group, those receiving the memory reframing intervention showed significant reductions in distress at a subsequent lumbar puncture 1 week later. Similarly, Pickrell and colleagues examined the effectiveness of a memory reframing intervention among children (aged 6–9 years) undergoing repeated restorative dental treatments involving local anesthesia injections [36]. At 2 weeks following the initial dental treatment, children were randomized to receive either a memory reframing intervention, which was designed to positively reframe their memories of the previous procedure, or an interactive neutral discussion (i.e., control condition) led by an interventionist. Immediately following the intervention or control procedure, children

once again underwent a similar dental treatment. Findings revealed that children receiving the memory reframing intervention, as compared with children in the control group, remembered experiencing less pain and fear than they actually reported at the initial procedure, reported less fear following injections over time, and showed improvements in their behavior (i.e., degree of cooperativeness) from the first to the second dental treatment.

Given these findings, it is surprising that more research has not examined the effectiveness of similar memory reframing interventions for use with other pediatric populations (e.g., healthy children and children with anxiety disorders). Given the powerful role of parents in shaping children's pain experience/expression [37–39], as well as their autobiographical memories [3,40], parent-led memory reframing interventions may be particularly promising and cost effective. Moreover, given the frequency with which parent–child interactions take place in children's naturalistic environments, there would be a wealth of opportunities for verbal interactions between parents and children aimed at positively reconstructing pain memories.

In addition to the influence of postevent information on the reconstruction of children's pain memories and subsequent pain experience, there is a small body of experimental research suggesting that provision of information prior to a novel event (e.g., visiting a pretend zoo or a pirate) can have a significant impact on the accuracy and completeness of children's autobiographical memories [41–43]. Moreover, there is theoretical support for the role of information provision prior to medical procedures in promoting more accurate expectations and schemas – based on children's previous experiences and memories – as well as optimal emotion regulation and coping [44]. Given that more accurate pain memories are linked to less pain and anxiety during subsequent painful experiences [10,11], future research should examine the influence of pre-event information provision and children's pain memories and experiences over time.

A preliminary model of acute pain memory development in childhood

The results of the extant research on children's memories for pain have important theoretical and clinical implications and enhance our understanding of the factors that influence

the development of children's pain memories from their inception, their reconstruction over time, and the manner in which these memories shape subsequent pain experience. A preliminary empirically and theoretically derived model of how these factors are hypothesized to influence pain memories, and how pain memories influence subsequent pain experiences, is presented in **Figure 1**. Consistent with predictions of theories of anxiety and memory biases [32,45], children with higher levels of anxiety and danger-related schemata pertaining to their general environments and somatic sensations tend to develop pain memories that are characterized by amplified estimations of sensory and affective threat over time. Several theories also predict that these memories develop as a result of highly anxious children's attentional biases toward threatening aspects of the painful experience [32,46]; however, it is also possible that there are subtypes of highly anxious children who differ in their individual attention style (e.g., hypervigilant versus avoidant of threat cues) and who may also differ in the degree to which their memories become negatively estimated over time [47]. It is likely that in addition to general anxiety-related constructs (e.g., state/trait anxiety and anxiety sensitivity), the presence of fear and anxiety that is specific to pain itself (e.g., fear of pain, pain anxiety and pain catastrophizing) is strongly related to memory biases. Furthermore, these general anxiety-related variables are thought to be predisposing factors that predict the development and exacerbation of pain-specific fear and anxiety (e.g., fear of pain and pain catastrophizing) [48–51]. Highly anxious children are also likely to be characterized by a perceived inability to cope with pain [45], which could influence the construction and reconstruction of pain memories at encoding and retrieval, as well as the development of negative expectancies of future pain. Indeed, negative memory biases, such as the anxiety constructs described herein, are characterized by amplified estimations of threat; that is, highly anxious children recall their experience as more painful and fear-inducing than they initially report it to be. Once these negative memory biases develop, they become powerful predictors of children's subsequent pain experience. It has been suggested that negative memory biases and pain expectancies seen among highly anxious and fearful children may become activated upon re-entry into the

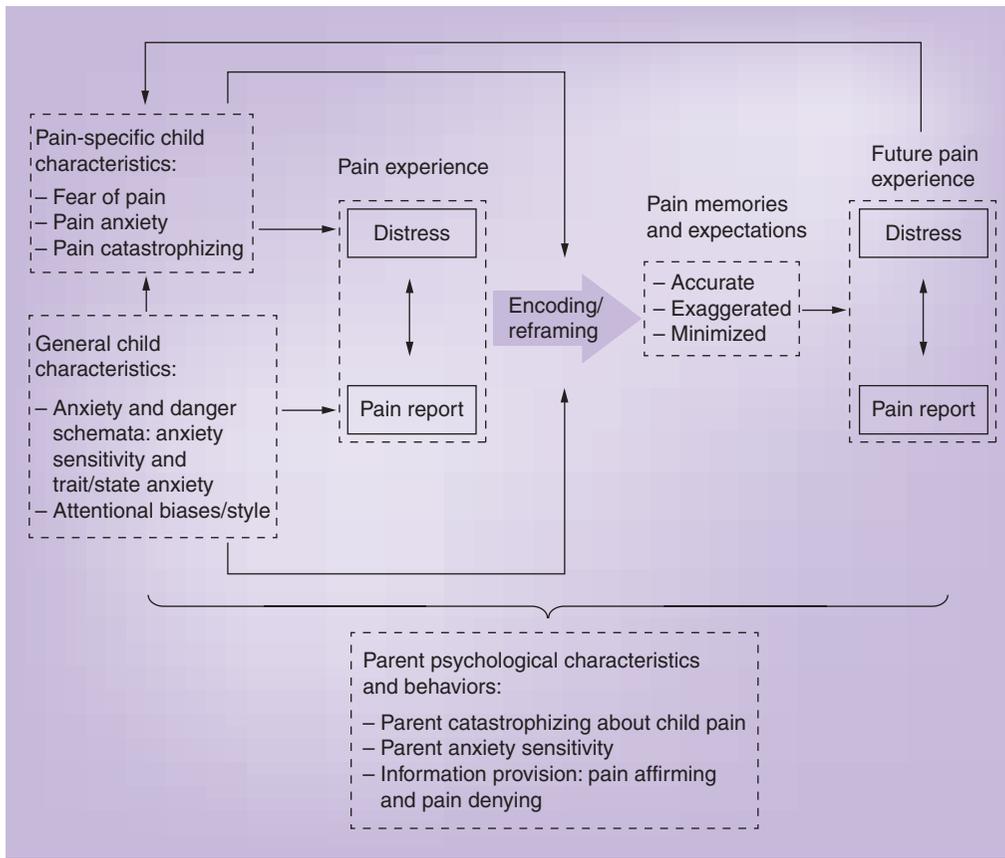


Figure 1. A preliminary model of acute pain memory development in childhood outlining the theoretically and empirically derived relationships between child and parent factors that are hypothesized to influence the development of children's pain memories, expectations and pain experiences over time.

pain context and then further exaggerated as a result of increased arousal [10]. As a result, negatively estimated memories and expectancies likely become the experiential context through which subsequent pain is experienced. Not surprisingly then, these children's reactions to pain, like their pain memories themselves, come to involve even more distress over time. Furthermore, this process likely exacerbates and perpetuates the vicious cycle of increased pain-specific anxiety and fear, distress, pain during painful experiences, additional reconstruction of negatively estimated pain memories and expectancies, and heightened subjective reactivity to pain over time.

To date, research on children's memories for pain has seldom examined the role of parents. Nevertheless, children do not live and experience pain in isolation; indeed, parents exert a powerful influence on the socialization of children's fear, anxiety, memory and pain behaviors [3,37–40,52]. Children's beliefs

and cognitions about the inherent threat value of pain develop within the familial context. Through early vicarious and instrumental learning about somatic symptoms (including pain), individuals develop beliefs and cognitions about the dangerousness of pain and the appropriateness of associated behaviors [53–57]. Similarly, children's autobiographical memories develop within this familial context and are highly influenced by the quality and content of their verbal interactions with individuals in their social environments, particularly parents [3,40]. Cognitive affective parent factors shown to increase child pain behaviors and anxiety, such as parental catastrophizing about child pain [58,59] and parental anxiety sensitivity [60], likely fuel the complex inter-relationships between parent and child factors in influencing the development of pain memories and subsequent response to pain. Moreover, the relationships between the psychological characteristics and behaviors of the parent and those of the

child are likely reciprocal [61,62]; as such, parents can exert influence at every stage in the cycle. Accordingly, they have the potential to be critical agents in intervention efforts aimed at reducing children's anxiety before, and fear and pain during, painful experiences. Furthermore, they have the potential to influence the reframing of children's pain memories and modification of expectancies through parent-child discourse following painful experiences.

Conclusion & future perspective

Researching children's memories is not without its methodological challenges (e.g., difficulty disentangling memory of pain experience from memory of pain reporting, necessity of reliance on self-report and lack of control over factors influencing memory reconstruction over time); however, the importance of understanding the development of pain memories and their influence on children's experience of pain over time cannot be overstated. The recent development of child and parent report measures of pain-related fear and anxiety [48,63,64] will enable more refined examinations of the role of anxiety and fear in the development of children's pain memories. The development of the pediatric fear-avoidance model of chronic pain [62] – an adaptation of Vlaeyen and Linton's model to explain the processes by which pain transitions from an acute to a chronic state [65] – provides intriguing opportunities to examine the role of cognitive and affective fear-avoidance factors in both the child's pain experience and the development of their pain memories over time. Furthermore, given that the mediating role of attention is at the core of theories put forth to account for the relationship between anxiety and memory biases [32], inclusion of measures of attention in future investigations is warranted. Finally, multimethod investigations of the reciprocal influences of parent and child psychological factors in the development of pain memories and coping over time will offer valuable insights that will facilitate the ultimate goal of improved pain management for children. Although intriguing questions about the nature of children's pain memory development exist, and research is needed to disentangle its inherent complexity, such future research offers promise for improved identification, assessment and treatment of children at risk of developing pain memories that can have important implications for their health across the lifespan.

Acknowledgements

Parts of this review paper are derived from unpublished portions of the first author's doctoral dissertation entitled, 'Children's memory for pain: experimental investigations of the role of anxiety in children's pain memories and the influence of pain memories on subsequent pain experience'. The authors greatly appreciate the generosity of the anonymous reviewer who made important contributions to the development of the preliminary model. The authors would also like to thank K Birnie and K Boerner for their valuable insights into the model. Finally, the authors would like to sincerely thank the children and families who took part in this dissertation research and inspired these ideas and writing.

Financial & competing interests disclosure

M Noel and M Petter are Killam Scholars and are supported by Frederick Banting and Charles Best Canada Graduate Scholarships Doctoral Awards from the Canadian Institutes of Health Research (CIHR). At the time that this work was completed, M Noel was also supported by a CIHR Team in Children's Pain Fellowship. M Noel's dissertation research was supported by a Marion and Donald Routh Student Research Grant from the Society of Pediatric Psychology (Division 54, American Psychological Association), a Canadian Pain Society Trainee Research Award from the Canadian Pain Society, and a Category A Research Grant from the IWK Health Centre awarded to M Noel. Funding for this research was also provided by an operating grant from the CIHR and infrastructure funding from the Canada Foundation for Innovation awarded to CT Chambers. M Noel and M Petter are trainee members of Pain in Child Health, a Strategic Training Initiative in Health Research of CIHR. CT Chambers and PJ McGrath are supported by Canada Research Chairs. SH Stewart was supported through a Killam Research Professorship from the Dalhousie University Faculty of Science at the time this research was conducted. The authors have no other relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript apart from those disclosed.

No writing assistance was utilized in the production of this manuscript.

Ethical conduct of research

The authors state that they have obtained appropriate institutional review board approval or have followed the principles outlined in the Declaration of Helsinki for all human or animal experimental investigations that they conducted themselves. In addition, for investigations involving human subjects that they themselves conducted, informed consent has been obtained from the participants involved.

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