Traumatic Stress and Pediatric Pain: Towards a Neurobiological Stress-Health Perspective

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Published online: 17 April 2017
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Abstract This theoretical review aims to present the limited findings on traumatic stress and pain in children and adolescents, highlight recent discoveries regarding neurobiological processes, and suggest an alternative stress-health perspective in the future study and conceptualization of pediatric pain and traumatic stress based on results. Current literature highlights a positive correlation between pain and trauma symptoms in youth and suggests a complex relationship that may have mutually maintaining dynamics and intertwined physiological processes. Developmentally sensitive, longitudinal, process-oriented designs assessing neurobiological alterations and stress responses should be utilized in the examination of the trauma-pain relationship. Such investigations may provide a more unified explanation of the relationship between chronic pain and traumatic stress.

Keywords Traumatic stress · Pain · Children · Adolescents · Neurobiology

For many individuals, and especially children and adolescents, experiencing pain can be stressful and even

traumatizing. Though often thought of as separate constructs that, at most, simply affect each other, empirical findings may point towards a more intricately connected stress mechanism for the occurrence of both pain and trauma symptoms. In the present theoretical review, we present findings that prompt the consideration of such an alternative perspective in the future study and conceptualization of pediatric pain and traumatic stress.

Traumatic Stress and Pain

The correlation between traumatic stress and pain is well-documented among adults, though exact mechanisms are still unclear (Asmundson and Katz 2009; Asmundson et al. 2002; Kulich et al. 2000; Otis et al. 2003; Sharp and Harvey 2001). In children and adolescents, this link is even less understood. Here we begin to examine the limited findings on trauma and pain in children and adolescents to heighten understanding of these seemingly overlapping processes.

Definition of Terms

“Traumatic stress” is operationally defined, in accordance with The National Child Traumatic Stress Network’s explanation, as the disruptions in equilibrium and homeostasis that occur when exposure to traumatic events or situations overwhelms a child’s or adolescent’s ability to cope (The National Child Traumatic Stress Network 2014; Traumatic Stress 2010). Posttraumatic stress disorder (PTSD) is defined by the criteria listed in the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5) and understood as assuming exposure to a traumatic event, with experience of symptoms of traumatic stress (e.g., intrusive symptoms, avoidance) (American Psychiatric Association 2013). As

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such, pediatric PTSD, medical, complex, and interpersonal traumatic stress types (e.g., injury, abuse) were all included in our conceptualization of “traumatic stress.”

Pain becomes increasingly problematic and debilitating when it transitions from being acute to chronic. Our review draws from both acute and chronic pain literature in examination of traumatic stress’s impact on pain and especially, pain chronicization. Chronic pain is defined as pain persisting for 3 months or longer (International Association for the Study of Pain 2014) and is increasingly recognized as a major health concern among youth, with prevalence rates rising in the past several decades (Ho et al. 2008; King et al. 2011). Although the exact pathways for chronic pain development and maintenance remain elusive, there is evidence that the process includes physiological and psychological factors such as trauma history (Casey et al. 2008).

Co-Occurrence of Pain and Trauma Symptoms

Several reviews have indicated high co-occurrence of traumatic stress and chronic pain among adults; specifically, increased prevalence of chronic pain has been found in patients with PTSD (Asmundson and Katz 2009; Asmundson et al. 2002; Kulich et al. 2000; Otis et al. 2003; Sharp and Harvey 2001). Alternatively, pain symptoms were also found to predict PTSD development (Norman et al. 2008). In fact, a national comorbidity study indicated that patients with musculoskeletal pain are four times more likely to develop PTSD than those without (Cox and McWilliams 2002). In light of these findings, researchers have asserted the importance of recognizing the co-prevalence of PTSD and pain for treatment development (Clapp et al. 2009).

Childhood history of traumatic stress has also been found to predict pain symptoms in adulthood (Casey et al. 2008; Goldberg and Goldstein 2000). A meta-analysis found that reports of abusive or neglectful childhood experiences predicted elevated risk for chronic pain in adulthood (Davis et al. 2005). Similarly, multiple reviews have affirmed the relationship between childhood abuse and chronic pain disorders in adulthood (Hart-Johnson and Green 2012; Walsh et al. 2007; Wuest et al. 2008). In a young adult population (mean age = 22), individuals with chronic pain were found to be more likely to report history of sexual abuse, even after controlling for depressive symptoms (Brown et al. 2005). Consistent with these results, a national comorbidity survey found that those who reported a health problem as well as experiences of childhood trauma (e.g., physical and sexual abuse) reported more pain than those who did not report such histories (Sachs-Ericsson et al. 2007). In a pilot functional magnetic resonance imaging (fMRI) study conducted with adults diagnosed with multisomatoform pain disorder and matching control group, researchers uncovered higher activations in the left lateral and medial superior frontal gyrus in response to pain stimuli among those with a history of abuse

(Noll-Hussong et al. 2010). This suggests differences may exist or develop at a neurobiological level secondary to a history of traumatic stress and/or abuse.

Existing Models for the Co-Occurrence of Pain and Trauma

In general, neurobiological models implicate altered physiology resulting from traumatic stress as a contributor to chronic pain development. They propose that trauma exposure triggers a cascade of neurobiological changes that culminates in a state of neural hyperresponsivity (i.e., symptoms of hyperarousal and vigilance) associated with both chronic pain and PTSD (Garkinfel and Liberzon 2009; Rahn et al. 2013). Multiple reviews have specifically implicated the amygdala in PTSD and chronic pain symptom development (Garkinfel and Liberzon 2009; Simons et al. 2014a). Scioli-Salter et al. (2014) reviewed the shared neurobiology of comorbid chronic pain and PTSD, and noted the convergence of circuits that mediate emotional distress and physiological threat (with specific mention of factors such as neuropeptide Y and neuroactive steroids) implicated in the pathophysiology of both conditions.

On a broader level, Sharp and Harvey (2001) argued that chronic pain and PTSD could be conceptualized as mutually maintaining conditions. The authors posited that cognitive, affective, and behavioral components of chronic pain might exacerbate and maintain PTSD, leading individuals to experience and/or interpret pain as a salient reminder of trauma. Similarly, they suggested physiological, affective, and avoidance components of PTSD may exacerbate and maintain pain symptoms. Asmundson et al. (2002) described a shared vulnerability model of chronic pain and PTSD, with anxiety sensitivity serving as the common predisposing factor for both chronic pain and PTSD development.

Notably, Asmundson et al. (2012) also proposed a pediatric-specific fear-avoidance model of chronic pain that implicates child as well as parental factors. This is a multifaceted paradigm in which the child’s pain experience and response are influenced by fear and avoidance behaviors, which in turn affect caregiver responses and pain management behaviors, and exacerbate further avoidance. The model addressed bidirectional influences of parent behaviors and pain-related fear and avoidance, and proposed that decreased fear leads to exposure and recovery. From a trauma perspective, fear and avoidance are hallmark features of a traumatic stress response, and a positive correlation between traumatic stress and chronic pain is consistent with the pediatric fear-avoidance model.

A Closer Look in Pediatric Populations

The link between traumatic stress and pain occurrence in youth has otherwise only been peripherally examined,

prompting this exploratory review of literature. Studies conducted within the past decade examining both traumatic stress/PTSD and pain maintenance in child and/or adolescent samples were systematically identified and reviewed. Articles examining traumatic stress and neurobiological alterations, as well as chronic pain and neurobiological alterations, were also separately reviewed. Result themes are presented below.

Traumatic Stress and Pain in Youth as Main Variables of Study

Studies directly examining traumatic stress or PTSD and pain in youth samples are few but, like in adult samples, point toward a significant relationship. In a review of chronic posttraumatic headache (CPTHA) in children, Goryunova (2011) noted the seemingly independent nature of headache intensity from severity of craniocerebral trauma. Instead, the author posited that pain chronicity is linked to multiple factors including psychologically traumatizing social contexts. Seng et al. (2005) uncovered significant comorbidity between various chronic pain conditions (e.g., pelvic pain, fibromyalgia, irritable bowel syndrome) and PTSD in an epidemiological service-use study conducted among females ages 0–17 years ($n = 1672$) utilizing Medicaid benefits. Among these female youth with a PTSD diagnosis, over 56% also had diagnostic codes for chronic fatigue, fibromyalgia, irritable bowel syndrome, chronic pelvic pain, or dysmenorrhea denoted in their medical records.

Impact of Traumatic Stress on Pain Sensitivity and Processing

Search results revealed a few studies that examined trauma in the forms of bodily injury or acute medical conditions (e.g., burns, traumatic brain injury) with long-term effects on pain sensitivity and processing that affect chronic pain development. Traumatic stress incurred through these events entails limitations in coping with the injury/condition (whether the pain itself or ramifications of the event).

Wollgarten-Hadamek et al. (2009) found global changes in pain sensitivity over time among 48 school-age children, ages 9–16, with histories of burn injuries in infancy. Results suggest that early traumatic injuries can induce long-term changes in later pain experiences. The authors consequently highlighted the need to build evidence regarding the impact of early stress on pain processing aside from nociceptive input. Though this particular study did not directly assess PTSD symptomatology, other studies have found substantial prevalence of PTSD in young children with burns (Graf et al. 2011; Saxe et al. 2005), supporting strong likelihood of traumatic stress experience from burn injuries.

A similar process of pain maintenance after traumatic injury has also been observed in children and adolescents with histories of traumatic brain injury (TBI). Brown et al. (2014)

tested three models (i.e., the mutual maintenance, pain, and perpetual avoidance models) in a sample of 195 children, ages 6–15, who presented following mild to severe TBI. The mutual maintenance model proposes shared perpetuation of pain and PTSD symptoms (Liedl et al. 2010; Sharp and Harvey 2001). The pain model contends that pain perpetuates PTSD unidirectionally (Norman et al. 2008), while the perpetual avoidance model posits that PTSD facilitates the maintenance of pain (Liedl and Knaevelsrud 2008). Analyses supported the mutual maintenance model and nested perpetual avoidance models, suggesting that PTSD may drive the presence of pain and not vice versa. As a result, the authors suggest the post-traumatic maintenance model: posttraumatic distress influences bodily pain unidirectionally.

Tham et al. (2013) identified predictors of persistent pain in a sample of adolescents, ages 14–17 years old, with TBI. Authors followed 144 adolescents with mild to severe TBI over 36 months, and persistent pain was identified in adolescents who provided pain intensity ratings of 3/10 or higher at four separate assessment points. PTSD symptoms were specifically examined, and adolescents with persistent pain endorsed significantly higher levels of PTSD symptomatology at 3 and 36 months compared to adolescents with infrequent pain. The investigators noted that injury may affect neuronal hyperexcitability and hyperreactivity, and/or contribute to changes in brain regions previously associated with chronic pain (Tham et al. 2013; Turner and Levine 2008).

In a review of anxiety among youth with medical conditions, authors summarized the relationship between painful medical interventions and PTSD, suggesting lasting effects of painful procedures on later pain processing (Pao and Bosk 2011). Further, in a review of complex traumatic stress in the medical setting, traumatic stress was described to influence pain maintenance via mechanisms of emotion dysregulation, information processing, and dissociation (Brosbe et al. 2013).

Neurobiological Factors

Changes in pain sensitivity and processing predicted by traumatic stress yield questions regarding the neurobiological alterations that may contribute to this link; however, few studies have examined this in a child and/or adolescent population. Simons et al. (2014b) found that pediatric patients with complex regional pain syndrome (CRPS) – a chronic pain syndrome involving neuropathic pain, changes in limb perfusion, and decreased ability to use the extremity (Harden et al. 2013) – showed *increased* connectivity of a number of brain areas. Regions included the prefrontal cortex, motor areas, bilateral middle cingulate, and left amygdala regions. The latter region is generally reflective of areas traditionally associated with increased fear and avoidance responses. Connectivity *decreased* in these areas following treatment for CRPS (Simons et al. 2014b). Hypersensitivity

and hyperarousal may explicitly be associated with these connectivity alterations, as the amygdala is largely responsible for activating the hypothalamus-pituitary-adrenal (HPA) axis that triggers stress responses (Lupien et al. 2009).

Though findings are not exclusive to a pediatric population, deficits in the brain's abilities to inhibit amygdala arousal in individuals with PTSD have similarly been identified (Nutt and Malizia 2004). Pediatric PTSD and early life stress *has* been associated with increased amygdala reactivity to negative stimuli as well as changes in hippocampal volume (Dannlowski et al. 2012) and impaired prefrontal inhibition (Roozendaal et al. 2009). Essentially, the connectivity changes observed in pediatric CRPS patients (as mentioned above) bear resemblance to similar alterations in individuals with PTSD and history of trauma, suggesting possible overlapping processes, which warrants further clarification via imaging studies within a pediatric population.

It should be noted that the studies reviewed above examined chronic pain in relation to traumatic stress as tied to an identifiable event(s); however, traumatic event history is not always present in chronic pain development. Thus, the possibility of neurobiological alterations occurring without the presence of an identifiable traumatic event or existence of an alternate pathway of chronic pain development in these cases should also be considered. For example, studies on young women entering puberty suggest persistent neuronal and hormonal changes associated with increased mood lability, as well as increased pain (Oldehinkel et al. 2011; Rapkin et al. 2006). One possibility may be that the persistent re-experiencing of pain may serve as the source of traumatic stress in and of itself. Known pain amplifiers such as catastrophizing (e.g., repeatedly thinking about painful events), parental overprotection (e.g., frequently checking on levels of discomfort), and limited social support (e.g., isolation leading to affective distress that further sensitizes the nervous system to discomfort; rejection by peers who do not validate chronic pain as a “real” medical condition) may further exacerbate the pain cycle by release of pro-inflammatory cytokine, interleukin-6 (IL-6) and heightening the overall distress response (Edwards 2008). These variables may synergistically feed pain processes, leading to micro-traumas each and every time the child reflects back on acute pain flares, has a caregiver remind them of a recent event leading to heightened discomfort, and/or when peers make unsupportive comments about their vulnerabilities with chronic discomfort. Micro-traumas may thus lead to further pain exacerbations via heightened neurobiological reactivity. In fact, parts of the neural system dedicated to the detection of physical pain, the dorsal anterior cingulate cortex (dACC) and anterior insula (AI), have been suggested to serve as a “neural alarm system” for social cues in adolescents, suggesting a direct influence of social factors on neural structures involved in pain processing (Dalgleish et al. 2017).

Amygdala activation and stimulation of fear and avoidance responses in chronic pain patients are consistent with findings documenting the role of children's fear-related pain memories that affect subsequent reactions to pain (Noel et al. 2012; Noel et al. 2015). Pain memories may serve as a potent reminder of trauma, triggering arousal responses and avoidance behaviors, consistent with both the pediatric fear-avoidance and mutual maintenance models. Researchers and clinicians alike have suggested treating pain by erasing fear memory traces in order to mitigate the role of pain memories on the maintenance of pain chronicity. In fact, researchers propose that the neuronal mechanism for memory formation itself appears to be instrumental for the development of pathological forms of both pain and fear, and perhaps trauma symptoms as well (Sandkuhler and Lee 2013). In support, the somatosensory cortex, considered the main site for pain perception has been noted to contribute to memory formation through the process of conditioning and associative learning (Diesch and Flor 2007; Prakash and Golwala 2011).

Towards a Neurobiological Stress-Health Perspective

The current theoretical review sheds light on an empirical yet under-examined relationship between traumatic stress and pain perception changes in youth who develop chronic pain. Given the body of literature in the adult population and promising findings with pediatric samples, neurobiological mechanisms, specifically amygdala activation processes and associations with hippocampal memory processes, may serve as a unifying lens across models in explaining the trauma-pain relationship. Understanding these mechanisms, and how developmental stages mediate them, may help practitioners determine if, when, and how traumatic stress could distinguish individuals at risk for chronic pain development.

A neurobiological, process-oriented understanding of chronic pain – how it develops and how it is maintained – may also better inform practitioner perspectives. Questions regarding whether a patient experiencing chronic pain is managing a somatic experience hindered by traumatic stress, exhibiting a faulty signaling system triggering recurrent trauma, or evidencing a purely psychological inability to cope with unaddressed needs may be explored. Such investigations are imperative for informing clinical conceptualizations of chronic pain to optimize treatment and provide necessary support for pediatric chronic pain patients.

Pediatric trauma, traumatic stress, and pain have historically been viewed as separate constructs with distinct bodies of research literature. Findings suggest that chronic pain and PTSD could be viewed as related states of hyperarousal of the central nervous system and exaggerated neuronal responses to stress triggers. Responses are likely related to neurobiological changes in brain connectivity, HPA axis

responsiveness, and even epigenetic changes that modulate gene expression, an area ripe for additional examination (Rahn et al. 2013; Teicher et al. 2002).

In the same vein, altered physiological processing and effects on sensitivity and pain perception may be viewed as responses to traumatic stress over time. Studies cite lasting differences in pain thresholds with early stress experiences (Wollgarten-Hadamek et al. 2009), evidence for PTSD driving pain perpetuation, and persistent pain correlated with higher reports of PTSD symptoms (Tham et al. 2013). Examination of trauma's impact on pain sensitivity and processing in youth has focused mainly on traumatic injury, yet researchers suggest that various forms of early life stress can have a lasting impact on physiology (Bartholomeusz, Callister, & Hodgson, 2013). The distinction, then, between changes in pain processing due to physical injury or distressing nociceptive input versus traumatic stress alone should be clarified.

Importantly, in examining the pediatric population, developmental factors must also be prominently considered. Child trauma and stress literature suggest that children are affected differently by traumatic stress at different stages of development (Van der Kolk 2003). For example, in prenatal stages and early childhood, mothers' psychological states and parent-child interactions influence HPA axis programming in the child (Kuhlman et al. 2015; Laurent et al. 2014), while in adolescence, research indicates increased sensitivity to elevated levels of stress hormones (e.g., earlier exposures to stress become evident in the form of high glucocorticoid levels (Lupien et al. 2009)). These distinctions, overall, may contribute to if and how chronic pain develops across the lifespan (e.g., higher glucocorticoid sensitivity during adolescence as a potential contribution to the higher prevalence of chronic pain in this age group) (King et al. 2011; Oldehinkel et al. 2011); Rapkin et al. 2006).

Additional research is imperative in order to better denote the validity of overlapping neurobiological pathways for trauma and pain symptoms. Importantly, the impact of early stress on the developing brain in infants, children and adolescents may be distinct from processes observed in the adult population. Developmentally sensitive and longitudinal, process-oriented designs assessing neurobiological alterations and stress responses should be utilized in conjunction with ongoing outcomes research examining specific components of the trauma-pain relationship.

Conclusion

Current literature highlights the association between pain and trauma symptoms in children and adolescents; however, most publications examine trauma pediatric medical stress as single incidents surrounding the traumatic event rather than with longitudinal and developmentally-sensitive, process-oriented

designs. Still, the connections and patterns identified provide substantial basis for future research directions in common neurobiological processes.

More broadly, findings point toward complex connections between pain and traumatic stress symptoms. Future researchers may consider neurobiology and stress responses as common mechanisms for both pain and trauma symptoms (and their attenuation). The overlap would warrant a more unified approach to research with pain and trauma symptoms recognized as two arms of the human stress response. Collaborative investigations and interventions for stress may then be seen as preventive and effective for trauma disorders and chronic pain. Overall, enhancing understanding of neurobiological stress responses in youth and their manifestations may lead to an important stroke in painting the picture of how chronic pain and traumatic stress develop and relate.

Acknowledgements, Informed Consent and Conflict of Interest

We, the undersigned authors, certify that we have no commercial associations (e.g., consultancies, stock ownership, equity interests, patent-licensing arrangements, etc.) that might pose a conflict of interest in connection with the submitted article. No funding sources supporting the work and all institutional or corporate affiliations were utilized. We also certify that the submitted article contains no descriptions of individuals, family history, and/or photographs in which a person's identity can be recognized. The present work has not been published elsewhere and that has not been submitted simultaneously for publication elsewhere.

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