

# The relationship between traumatic exposure and pain perception in children: the moderating role of posttraumatic symptoms

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## Abstract

Adverse childhood experiences (ACEs) affect approximately half of all children worldwide. These experiences have been linked to increased pain sensitivity in adulthood and a higher likelihood of developing severe chronic pain. However, most studies have assessed the effects of ACEs retrospectively, long after they occurred, leaving room for other factors to influence the observed outcomes. We investigated, for the first time, the association between ACEs and concurrent pain perception among young children who live in a conflict zone and are consistently exposed to potentially traumatic experiences. Participants were 60 elementary school children (ages 8–11 years) living in conflict regions ( $n = 39$ ) or nonconflict regions ( $n = 21$ ). Posttraumatic stress symptom (PTSS) severity, traumatic exposure, pressure pain threshold (PPT), and mechanical detection threshold (MDT) were measured. Trauma-exposed children had significantly lower PPT than did controls, but MDT was similar across groups. Pressure pain threshold correlated positively with proximity to the conflict zone and inversely with traumatic exposure magnitude and PTSS severity. In addition, PTSSs moderated the relationship between repeated traumatic exposure and PPT. Children with higher PTSS severity displayed pain hypersensitivity regardless of their traumatic exposure level, whereas in children with lower PTSS severity, greater traumatic exposure correlated with pain hypersensitivity. The results suggest that ACEs among children lead to concurrent pain hypersensitivity and distress and may put them at elevated risk of chronic pain early in life. In addition, our findings emphasize the need for identifying children with various PTSS levels to provide tailored interventions and mitigate the long-term negative effects of ACEs.

**Keywords:** Childhood adversity, Traumatic exposure, Pain perception, Children, Posttraumatic stress symptoms

## 1. Introduction

Adverse childhood experiences (ACEs) refer to traumatic incidents that took place before age 18 years and have significant long-term effects on health and well-being.<sup>58</sup> More than 50% of children worldwide have experienced at least one ACE,<sup>16,33</sup> and the impact of ACEs is closely linked with various physical and mental health disorders in adulthood.<sup>12,17,21,29</sup>

One frequent outcome of ACEs is chronic pain. Adults with chronic pain are more likely to have a history of childhood adversity (eg, physical abuse, road traffic accident, neglect, financial difficulties, family conflicts, parental divorce, illness/death in the family, or living in conflict zones) than is the general population.<sup>8,24,28,30,39,73</sup> Young adults with chronic pain often report more stressful life events than do those without chronic pain.<sup>53,56,79</sup> Moreover, individuals who have experienced childhood adversity display worse pain-related outcomes when coping with chronic pain.<sup>10,15</sup> For example, women who

experienced child maltreatment reported higher pain intensity and more pain locations than those who had not been maltreated.<sup>7,61,62</sup>

Not only are ACEs associated with chronic pain in adulthood but also they have been linked with altered pain perception in adulthood. However, studies on this topic are scarce. For example, pressure pain threshold (PPT) was lower among adults with chronic back pain and a history of childhood maltreatment than it was among pain-free adults.<sup>70</sup> Pressure pain threshold was also lower among women with gastrointestinal pain disorders and a history of sexual/physical abuse than among nonabused women.<sup>62</sup> Early life stressors have also been associated with lower cold-pain thresholds in young adults experiencing current pain<sup>75</sup> and lower heat-pain tolerance in adult women.<sup>54</sup> Moreover, individuals who experienced high levels of childhood adversity demonstrated greater pain temporal summation,<sup>78</sup> and capsaicin-induced hypersensitivity than did those with low adversity.<sup>79</sup> Finally, pain-free adults with a history of ACEs perceived themselves as more pain sensitive than did those without such a history.<sup>64</sup>

Importantly, however, pain hypersensitivity in the aforementioned studies was recorded years after the ACEs occurred. Thus, many other factors (eg, age-related and morbidity-related changes) could have led to pain hypersensitivity. Furthermore, in many studies, the association between ACEs and pain perception was investigated among individuals with chronic pain, which in and of itself can alter pain perception, regardless of history. As pain hypersensitivity is considered a risk factor for chronic

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pain,<sup>5,23,32</sup> its early detection can promote preemptive interventions. Therefore, it is imperative and clinically relevant to study whether pain hypersensitivity already exists during childhood among children exposed to ACEs, an understudied research area. Moreover, although there is evidence in adults linking posttraumatic stress disorder (PTSD) with chronic pain<sup>6,17,56</sup> and altered pain perception,<sup>19,69,72</sup> we could not find studies assessing the role of posttraumatic stress symptoms (PTSSs) in the possible association between ACEs and concurrent pain perception among children.

The aims of this study were therefore to study (1) whether children exposed to potentially traumatic incidents exhibit concurrent hypersensitivity to noxious and/or innocuous stimuli compared with controls and (2) whether the severity of PTSSs moderates the relationship between level of traumatic exposure and pain sensitivity.

## 2. Methods

### 2.1. Participants

Sixty elementary-school children volunteered to participate in the study. The participants were randomly selected from different regions in the central and southern parts of the country, using snowball sampling. Although participants from both regions can potentially be exposed to ACEs in the form of conflict-related traumatic incidents, the southern region is closer to the border. Hence, it is subject to such traumatic exposure significantly more often (eg, missile attacks, incendiary balloons). Inclusion criteria were being between 8 and 11 years of age, no current pain syndromes, generally good health, and living in the same region for at least 3 years at testing time. None of the enrolled participants was physically injured or ill at the time of testing, and none had a present or past injury in the tested body regions. None of the participants used medications. The Institutional Review Board of Bar-Ilan University approved the study. After the procedure was fully explained to them, each participant and their parents signed informed consent.

### 2.2. Procedures

Sample sizes were calculated using G\*Power software.<sup>26</sup> Based on mean PPT values in our preliminary sample and in previous studies evaluating PPT among children<sup>35,80</sup> and their effect size, and based on the possibility of uneven group size (as it was more difficult to recruit age-matched controls), we conducted 2 a priori power analyses based on the ability to detect a medium effect size, with a 5% significance level ( $\alpha$ ) and 80% power level ( $1-\beta$ ).<sup>14</sup> The analysis for the *t* test yielded a need for a sample of 52 participants, whereas the analysis for the moderation model yielded a need for 48 participants. Considering that psychophysical testing might fail in approximately 15% of children, we recruited 63 children. Of this sample, 2 did not complete the entire data collection, and one was excluded due to equipment failure; therefore, the final sample included 60 children (see **Table 1** for a detailed sample description).

All participants were invited to a single testing session in which they underwent an interview, completed self-reported questionnaires, and underwent measurements of mechanical detection threshold (MDT) and PPT. These measurements were chosen for 3 reasons. First, we were interested in learning whether any changes in the participants' sensory sensitivity would be generalized (namely, affect both noxious and innocuous stimuli) or specific to the pain system. Second, the equipment used for

MDT and PPT is portable and less intimidating than the equipment required to measure thermal thresholds, especially for children. Third, a recent meta-analysis suggested that out of various experimental pain measurement previously tested, psychological trauma mainly affects the pain threshold.<sup>55</sup>

Before the actual measurements, the participants underwent a training session conducted on the forearm. The training was necessary to reduce stress, familiarize participants with the stimuli, and ensure that they understood the instructions and were relatively consistent in their responses. The participants sat upright in a comfortable chair with their arms supported. The training included explanations about the testing procedures and then 4 to 8 repetitions of the measurements on another body region (either the contralateral arm or the knee area). After a short break, the actual sensory testing commenced. The results were compared between children who live near the border of a conflict zone (<7 km) and hence experience multiple conflict-related traumatic exposures and children who do not reside near the border (>40 km from the border) and hence do not experience repeated traumatic exposure (control group).

### 2.3. Recording of posttraumatic symptoms, trauma exposure, and anxiety

The participants completed 3 questionnaires to assess the levels of traumatic exposure, posttraumatic symptoms, and anxiety severity.

The *Repeated Traumatic Exposure Questionnaire*<sup>47,74</sup> is a 10-item questionnaire assessing the level of ACEs in the form of repeated exposure to traumatic incidents. Each item describes a common conflict-related traumatic incident, modified to fit the common experiences of children living in Israel (eg, "I had to run to a secure space during a missile attack"). The participants were asked to rate the frequency of each incident in the past year on a 1 (*never*) to 6 (*at least once a week*) Likert scale.

The *Child Posttraumatic Stress Disorder (PTSD) Symptoms Scale for DSM-5 (CPSS5-I)*<sup>27</sup> is a 27-item interview that aims to assess PTSSs divided into 4 clusters of symptoms: intrusion (items 1-5), avoidance (items 6-7), changes in cognition and mood (items 8-14), and increased arousal and reactivity (items 15-20). Symptoms are ranked on a 0 to 4 Likert scale, resulting in a total severity score ranging from 0 to 80. Items 21 to 27 are used to calculate an impairment score ranging from 0 to 28.

The *Screen for Child Anxiety-Related Disorders (SCARED)*,<sup>9</sup> a 41-item inventory rated on a 0 to 2 Likert scale, aims to measure anxiety in children. It includes 6 subscales: panic disorder (eg, "When I get frightened, I feel like passing out"), generalized anxiety (eg, "I worry about being as good as other kids"), separation anxiety (eg, "I follow my mother or father wherever they go"), social anxiety (eg, "I feel nervous with people I do not know well"), and school avoidance (eg, "I get headaches when I am at school").

A well-trained psychologist administered both the CPSS5-I and the SCARED interviews.

### 2.4. Sensory testing

Mechanical stimuli for measuring MDT were delivered using Semmes-Weinstein monofilaments (North Coast Medical, Inc, Morgan Hill, CA). The kit consists of 20 monofilaments with sizes ranging between 1.65 and 6.65 units, each attached to a plastic holder. Vertical bending of the monofilament produces a calibrated force ranging between 0.008 and 300 grf. Mechanical detection threshold was tested using the modified method of

**Table 1**  
**Correlations between the experimental variables.**

	1	2	3	4	5	6
1. Pain threshold	1					
2. Border distance	0.29*	1				
3. Repeated exposure	-0.37**	-0.83**	1			
4. PTSD total	-0.21#	-0.28*	0.42**	1		
5. Daily functioning impairments	-0.34**	-0.29*	0.45**	0.55**	1	
6. Anxiety total	-0.20	-0.10	0.28*	0.63**	0.58**	1

Values are correlation coefficients. \* $P < 0.05$ , \*\* $P < 0.01$ .

limits. Although participants were blindfolded, the examiner applied the Semmes-Weinstein monofilaments on the dorsum of the hand in increasing order, starting from the smallest one (maximal range 0.064-1.143 mm). Participants were asked to respond the minute they perceived a touch, at which point they were asked to localize the stimulus perceived. Mechanical detection threshold was the calibrated force of the monofilament first perceived.<sup>61</sup>

Pressure stimuli for measuring PPT were delivered using a computerized pressure pain algometer (AlgoMed, Medoc Ltd, Ramat Ishay, Israel). The algometer consists of a handheld unit and a response unit and is operated through computer software that allows for real-time visual feedback for the examiner regarding the applied pressure so that a fixed pressure is applied during repeated stimulations (pressure units include kPa, Kgf/cm<sup>2</sup> and lbs/in<sup>2</sup>). Using the pressure algometer, the examiner exerts increasing vertical pressure on the skin at a constant rate, monitored and displayed on the computer screen. The tip of the algometer, which is pressed against the skin, was 1 cm<sup>2</sup> in diameter. A rate of 30 kPa was chosen, which was sufficiently slow to allow a precise recording of the participant's reaction while preventing the examiner from experiencing hand fatigue and preventing deviation from a constant rate of pressure increase. For PPT measurement, participants received 3 successive ramps of gradually increasing pressure on the forearm (about midway between the elbow and the wrist line) starting from a baseline of 0 kPa. For each ramp, participants were asked to press a switch (the response unit) when they first perceived pain, at which point the pressure was recorded and removed from the skin. Pressure pain threshold was computed by averaging the pressure readings of the 3 successive ramps.<sup>19</sup>

### 2.5. Data analysis

Data were processed with IBM SPSS statistics software (version 28). First, normal distribution was evaluated with the Kolmogorov-Smirnov (K-S) test. Participants were then divided into 2 groups in accordance with where they lived, indicating their distance from the border and hence exposure to potentially traumatic incidents. Parametric and nonparametric models were used to compare the demographics and sensory testing between children who lived near the border and were exposed to repeated traumatic incidents and children who lived in the central part of the country and were not repeatedly exposed to such experiences (control group). The independent demographic variables were age, gender, place of birth, place of residence, distance from the border, and number of children in the family. The sensory independent variables were MDT and PPT. Correlations between variables were assessed with 2-tailed Pearson *r* tests. We used independent samples 2-tailed *t*-tests to assess PPT and MDT as

a function of group type. Then, we used Hayes (2013) PROCESS macro using 5000 bootstraps resampling for calculating confidence intervals (model 1) to test the moderating role of PTSSs in the relationship between repeated exposure to trauma and PPT. Anxiety symptoms served as a control variable. *P* values < 0.05 were considered statistically significant.

## 3. Results

### 3.1. Characteristics of the sample

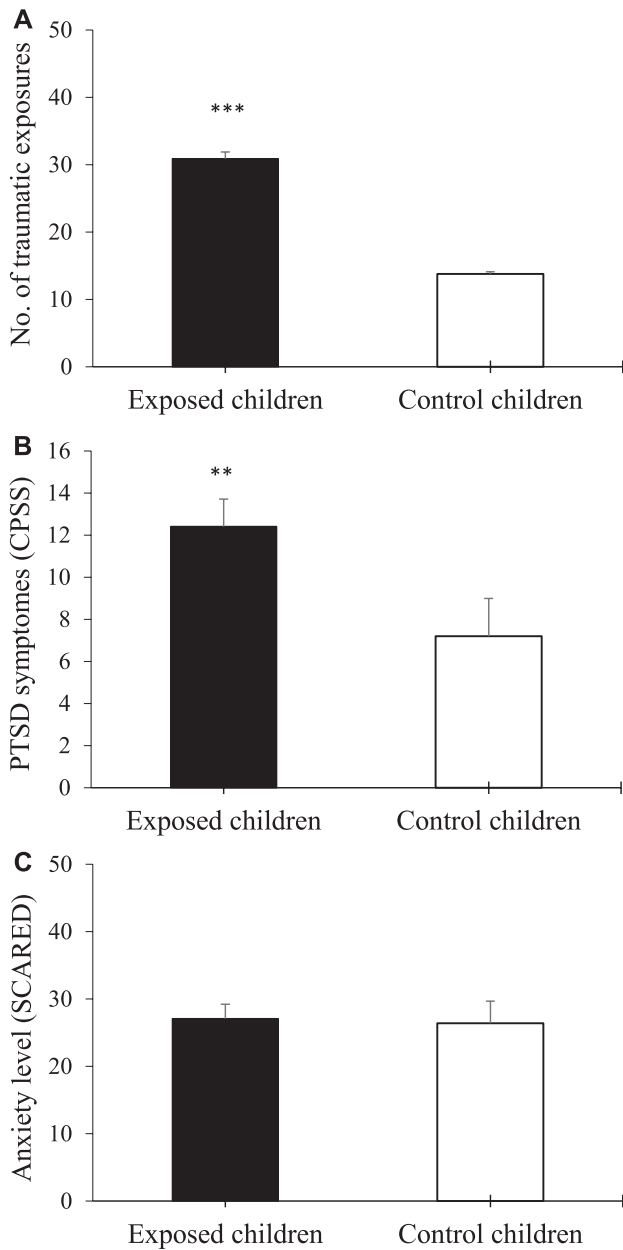
The sample included 60 boys and girls, of whom 39 lived in a conflict zone (exposed children) and 21 lived in a nonconflict zone (controls). The 2 groups did not differ in age (mean of 9.54 ± 1.24 and 9.71 ± 0.91 years, respectively), and gender distribution was similar among the groups: 19 boys (48.7%) and 9 boys (42.9%), respectively. However, children who lived in conflict zones experienced far more traumatic experiences than did controls (**Fig. 1A**) and had significantly more PTSSs than did controls (**Fig. 1B**). The 2 children groups did not differ in anxiety levels (**Fig. 1C**). There were no differences between boys and girls in PTSSs or anxiety,  $t(58) = 0.09$ ,  $P = 0.93$  and  $t(58) = 0.95$ ,  $P = 0.34$ , respectively.

### 3.2. Thresholds

We first conducted independent samples *t*-tests to compare MDT and PPT between female and male children, considering a possible sex effect on sensory testing. The analysis revealed a lack of gender effect on these thresholds,  $t(58) = 0.35$ ,  $P = 0.72$  and  $t(58) = -0.06$ ,  $P = 0.95$ , respectively. We then conducted an independent samples *t* test to compare MDT and PPT between exposed children and controls. The results revealed no significant difference between the groups in MDT,  $t(58) = 0.56$ ,  $P = 0.58$  (**Fig. 2A**). However, a significant difference between the groups was observed regarding PPT,  $t(58) = -2.29$ ,  $P = 0.026$  (mean difference -18.97, 95% CI: -35.5 to -2.38) (**Fig. 2B**). The results indicated that although there were no differences in mechanical detection, children who experienced repeated traumatic exposure had a significantly lower PPT than did controls.

### 3.3. Correlations between the thresholds and trauma-related variables

**Table 1** presents the correlations between PPT and trauma-related variables. As can be seen, there was a significant positive correlation between PPT and distance from the border, indicating that a shorter distance from the border was associated with lower pain thresholds. In addition, there were negative correlations

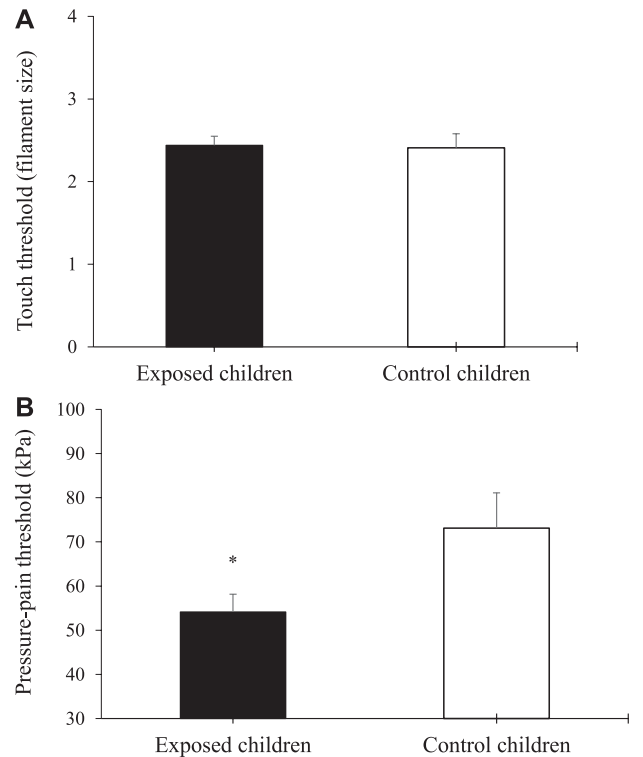


**Figure 1.** Children who live in conflict zones experienced a greater number of traumatic incidents than did controls (A) and exhibited more PTSDs than did controls (B); however, the 2 children groups did not differ in anxiety level (C). Bars denote group means and standard error (\*\* $P < 0.01$ , \*\*\* $P < 0.001$ ). CPSS, child posttraumatic stress symptom scale; PTSD, posttraumatic stress disorder; PTSS, posttraumatic stress symptom; SCARED, screen for child anxiety-related disorders.

between PPT, level of repeated traumatic exposure, and impairments in daily functioning, indicating that elevated levels of traumatic exposure and greater functioning impairments were associated with lower PPT. Finally, there was a marginal negative correlation ( $P < 0.1$ ) between PTSSs and PPT, indicating that greater PTSSs were associated with lower PPT.

**3.4. The moderating role of posttraumatic stress symptoms in the relationship between traumatic exposure and pressure pain threshold**

To examine the moderating role of PTSSs in the association between exposure to traumatic incidents and PPT in children, we conducted Hayes (2013) moderation model (model 1) with



**Figure 2.** Mechanical detection (touch) threshold was similar among exposed children and controls (A), whereas pressure pain threshold was significantly higher among exposed children than among controls (B). Bars denote group means and standard error (\* $P < 0.05$ ).

repeated traumatic exposure, PTSSs, and PPT as independent, moderator, and dependent variables, respectively. Anxiety symptoms, commonly associated with PTSSs, were entered as a control variable. The estimated coefficients of the main findings and their significance levels are described in **Table 2**.

The general model was significant ( $R^2 = 0.22$ ,  $F(3,55) = 3.81$ ,  $P = 0.008$ ). Importantly, there was a significant interaction between traumatic exposure and PTSSs. The interaction between exposure and PTSSs accounted for an additional 6.8% of the variance, above and beyond the variance explained by the main effects of exposure and PTSSs.

To interpret the interactive effects of repeated traumatic exposure and PTSSs on PPT, we computed bootstrapping

**Table 2**  
The relationship between repeated traumatic exposure, posttraumatic stress disorder symptoms, and pain threshold (estimated coefficients, standard errors, and 95% confidence intervals).

Variable	B	SE	t value	95% confidence interval	
				Low	high
<b>Predictors</b>					
Repeated traumatic exposure	-2.17	0.65	-3.35**	-3.47	-0.87
PTSD symptoms	-2.53	1.30	-1.95#	-5.13	0.07
Repeated exposure x PTSD	0.10	0.05	2.18*	0.01	0.19
<b>Control variable</b>					
Anxiety	-0.37	0.37	-1.01	-1.10	0.37

# $P < 0.1$ ; \* $P < 0.05$ ; \*\* $P < 0.005$ . PTSD symptoms as assessed by the CPSS-5; Anxiety symptoms as measured by the Screen for Child Anxiety Related Disorders (SCARED). B, unstandardized estimated coefficient; SE, standard error.

confidence intervals (95%) evaluating the magnitude of the relationship between repeated traumatic exposure and PPT for individuals with low ( $-1$  SD) and high levels of symptoms ( $+1$  SD) (Fig. 3). The analysis revealed that (1) among individuals with higher levels of posttraumatic symptoms, there was no relationship between traumatic exposure and PPT,  $t(59) = -0.13$ ,  $P = 0.90$ ; (2) among individuals with low levels of posttraumatic symptoms, there was a significant negative relationship between repeated traumatic exposure and PPT  $t(59) = -3.37$ ,  $P = 0.001$ , indicating that for these individuals, greater traumatic exposure was associated with increased pain sensitivity (lower PPT). Taken together, the results from the moderation model depicted in Figure 3 indicate that individuals with higher PTSS severity exhibit pain hypersensitivity, regardless of their level of traumatic exposure. Conversely, for those with lower PTSS severity, increased traumatic exposure is associated with heightened pain sensitivity.

#### 4. Discussion

The relationship between ACEs, PTSS severity, and pain perception was examined among young children with varying levels of concurrent traumatic exposure. Pressure pain threshold was lower among children undergoing repeated traumatic exposure than among controls; PPT correlated with the severity of traumatic exposure and proximity of residence to the conflict zone; PTSS severity influenced the association between trauma exposure and PPT. To the best of our knowledge, these results are reported here for the first time and contribute novel insights to the literature.

##### 4.1. Pain sensitivity among children exposed to traumatic incidents

The exposed children exhibited significantly greater sensitivity to noxious pressure than did the controls, but similar sensitivity to innocuous mechanical stimuli, suggesting that the alteration in sensitivity was specific to the pain system. We could not find studies assessing pain perception among pain-free children exposed to traumatic experiences. However, the present results correspond with studies on children with chronic pain. For example, compared with pain-free children, children and youth (ages 9-17 years) with chronic headache exhibited pain

hypersensitivity to mechanical<sup>67,80</sup> and thermal stimuli.<sup>54</sup> Children and youth with abdominal pain exhibited mechanical pain hypersensitivity<sup>25</sup> and alterations in pain modulation tests.<sup>11,52</sup> Children with severe burn injuries had attenuated stress-induced analgesia compared with those with moderate injury and controls.<sup>76</sup> Studies with larger samples reported heterogeneity in pain perception profiles of children and adolescents with chronic pain, possibly attributed to psychosocial variables.<sup>57,71</sup> Considering that chronic pain is a source of continuous distress,<sup>3,36</sup> these studies and the present results suggest that among children, psychological and/or physical trauma are linked with concurrent pain hypersensitivity.

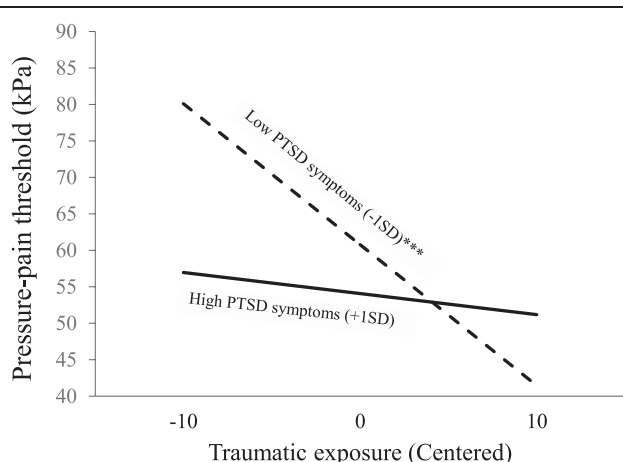
A recent meta-analysis focusing on adults has also acknowledged the potential pain-sensitizing effects of psychological trauma history. Based on 48 retrospective studies, the authors reported an association between trauma history and current pain hypersensitivity and/or hyperexcitability and concluded that trauma in general, and accumulated trauma specifically, increase the risk of chronic pain.<sup>55</sup> In this study, children living in conflict zones were constantly exposed to more traumatic incidents than were controls, hence subject to accumulated trauma. Importantly, PPT among these children correlated with their home's proximity to the border: The greater the proximity, the greater the pain hypersensitivity. Furthermore, PPT correlated with traumatic exposure level: The greater the exposure, the greater the pain hypersensitivity. The cumulative trauma effect of living in a conflict zone was thus reflected in the children's increased pain sensitivity. These results align with previous studies showing that repeated traumatic exposure affects daily functioning and impairs adaptive coping among various populations.<sup>34,46,47,68</sup>

Pain hypersensitivity may increase children's risk of developing chronic pain.<sup>5,23,32</sup> A previous study assessing pain, somatic symptoms, and trauma exposure among adults living in the same conflict zones, as children herein, provides insight into the children's possible futures. The study revealed a higher prevalence of chronic pain and greater pain severity among adults residing in conflict zones than those not residing there.<sup>4</sup> Other studies conducted among youth and adults with chronic pain reported more stressful life events than among those without chronic pain.<sup>8,24,28,30,53,56,73,81</sup> Altogether, these findings suggest that repeated traumatic incident exposure during childhood can lead to short-term and long-term alterations in the pain system.

##### 4.2. The moderating role of posttraumatic stress symptoms

Pressure pain threshold in this study correlated not only with conflict zone proximity and traumatic exposure level but also with daily functioning, and there were trends suggesting its correlation with PTSSs. Furthermore, exposed children had significantly greater PTSS severity yet similar anxiety levels compared with controls, reflecting a selective effect of trauma exposure. Most importantly, the moderation analysis revealed a complex interactive effect of trauma exposure and PTSS severity on PPT. Specifically, children with higher PTSS severity displayed pain hypersensitivity regardless of their traumatic exposure level. Conversely, children with lower PTSS severity experienced a positive association between traumatic exposure and PPT. Hence, greater traumatic exposure was associated with increased pain sensitivity.

Although one might expect that traumatic exposure leads to increased posttraumatic symptoms, which in turn lead to heightened sensitivity to stimuli, including pain,<sup>63</sup> these results reflect a more complex picture. It appears that high PTSS severity



**Figure 3.** The relationship between traumatic exposure and PPT in children with low ( $-1$  SD) vs children with high ( $+1$  SD) PTSD symptom severity ( $***P = 0.001$ ). PPT, pressure pain threshold; PTSD, posttraumatic stress disorder.

exerts such a substantial impact on children's pain sensitivity (perhaps leading to a ceiling effect) that environmental factors, such as traumatic exposure, have no additional influence. Conversely, children with lower levels of PTSSs are more vulnerable to developing pain hypersensitivity as their level of traumatic exposure increases. Hence, the analysis identified 2 risk factors among children living in conflict zones, namely, high PTSSs level or high exposure if PTSSs level is moderate, each of which may require a different treatment approach.

Although we could not find comparable findings in pain-free children, the complex relationship between PTSS severity and pain perception is demonstrated in the literature. For example, a study of youth with chronic pain revealed that greater PTSS severity was associated with both higher cold-pain tolerance threshold and higher pain catastrophizing.<sup>37</sup> A meta-analysis of the relationship between PTSD and pain perception in adults revealed inconsistent reports of either pain hypersensitivity or hyposensitivity.<sup>69</sup> Such inconsistency within a PTSD group has been explained by their different PTSS manifestation.<sup>20</sup> Finally, longitudinal studies revealed that PTSD trajectory mediated the association between trauma history and conditioned pain modulation,<sup>19</sup> and posttraumatic guilt mediated the associations between trauma history and pain threshold, pain tolerance, and pain temporal summation among adults.<sup>44</sup> Taken together, these results may support the idea that trauma exposure have differential effects on pain perceptions, depending on PTSS severity/manifestations.

The importance of identifying children at high risk of developing alterations in pain perception is well established. A recent review of prospective studies assessing the relationship between child maltreatment and chronic pain reported conflicting evidence across different maltreatment types; however, PTSD was identified as a potential mediator and/or moderator in this relationship.<sup>49</sup> Adults with a history of childhood abuse/neglect and PTSD had a significantly higher risk of pain complaints than those with either condition alone.<sup>61</sup> Moreover, PTSSs in the acute aftermath of trauma predict the presence and severity of chronic pain months later.<sup>18,38,48,50,66</sup> Thus, the children in this study seem to be at a particularly increased risk of developing chronic pain and pain-related disability, because of their pain hypersensitivity, their PTSSs, and their continuous traumatic exposure.

Although causality cannot be inferred from this study, animal studies provide strong support for causal relationship between early adversity and pain facilitation. For example, muscle mechanical hyperalgesia mediated by nociceptors' sensitization was recorded in adult rats exposed to neonatal stress.<sup>1,31</sup> Furthermore, stress-induced activation of the adrenal medulla,<sup>42</sup> as well as of spinal cord microglia<sup>65</sup> was responsible for long-term enhancement of muscle mechanical hyperalgesia. Thus, traumatic incidents can drive intracellular and extracellular cascades which, in turn, may increase the release of proinflammatory agents and alter the response properties of nociceptive neurons.<sup>2,13,22,40</sup> Such effects can result in pain system sensitization, which may underlie the low PPT observed herein. Reduced top-down prefrontal regulation over the amygdala and periaqueductal grey (PAG), observed in individuals with PTSD,<sup>43,45</sup> can further contribute to the observed hyperalgesia owing to the role of PAG in descending pain inhibition. Although the children herein were not diagnosed as having PTSD (ie, they experienced PTSSs), the presence of such symptoms can contribute to the aforementioned neuronal alterations and subsequent risks.<sup>41</sup> Given the repeated trauma exposure of living in a conflict zone and the children's age, sensitization and hyperalgesia may become permanent and highly increase the risk of concurrent and future chronic pain.<sup>55</sup>

### 4.3. Limitations and clinical implications

Although PTSS and anxiety symptoms were assessed using gold-standard interviews, traumatic exposure was assessed using a self-report questionnaire, which may have been subject to various influences, including the children's age. However, such influences are likely to occur among both groups. Second, we did not evaluate the threshold to thermal stimuli, which could provide additional information. As PPT was evaluated at a single site, a cautious interpretation is warranted. Nevertheless, the investment in a meticulous training session before PPT testing ensured a reliable performance among the children. Third, given the specific nature of the traumatic incidents, the results may not be generalized to all the known ACEs.

This study has several clinical implications. Since quantitative sensory testing (QST) can identify the risk of pain-related interference and chronic pain,<sup>51</sup> screening children undergoing ACEs with QST may promote early risk detection and tailoring interventions that may mitigate mental health problems and chronic pain in this group. Furthermore, early monitoring of PTSS among trauma-exposed children is important, as lower and higher symptom levels may require differential interventions given the current results. Thus, although the mere existence of PTSS poses a risk of mental health problems and pain facilitation,<sup>41</sup> children with lower PTSSs seem more vulnerable to concurrent traumatic exposure and, therefore may benefit more from interventions aimed to target this factor as compared to children with higher PTSSs. Furthermore, the results highlight the importance of identifying trauma-exposed children with moderate PTSSs, who may not necessarily seek treatment; however, they may still be at an increased risk of chronic pain if the traumatic exposure continues.

### Conflict of interest statement

The authors have no conflict of interest to declare.

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All coauthors have seen and agree with the contents of the manuscript, and there is no financial interest to report. The authors assure that authorship has been granted only to those who contributed substantially to the research or manuscript. The authors express their gratitude, respect, and support to the children who participated in this study and their parents.

The data of the study are available upon request.

### Supplemental video content

A video abstract associated with this article can be found on the PAIN Web site.

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