

Published in final edited form as:

Pain. 2012 February; 153(2): . doi:10.1016/j.pain.2011.11.004.

# Too sick for school? Parent influences on school functioning among children with chronic pain

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#### **Abstract**

Parental responses to children with chronic pain have been shown to influence the extent of the child's functional disability, but these associations have not been well-studied in relation to children's pain-related school functioning. The current study tests the hypothesis that parental pain catastrophizing and parental protective responses to child pain influence the extent of school impairment in children with chronic pain. A mediational model was tested to determine whether parental protective behaviors serve a mediating role between parental pain catastrophizing and child school impairment. Study participants were a clinical sample of 350 children ages 8-17 with chronic pain and their parents. Measures of pain characteristics, demographic characteristics, child depressive symptoms, school attendance rates, overall school functioning, parental pain catastrophizing and parental protective responses to pain were collected. Results show that, controlling for the known influences of pain intensity and child depressive symptoms, parental pain catastrophizing and parental protective responses to child pain each independently predict child school attendance rates and reports of overall school impairment. Parental protectiveness was found to mediate the association between parental cognitions (i.e. parent pain catastrophizing) and child school functioning outcomes. These findings underscore the importance of intervening with parents to foster parental responses to child pain that help children engage and succeed in the school environment despite pain.

#### **Keywords**

Chronic pain; Functional disability; Parents; Pediatric Pain; Psychosocial functioning; School functioning

#### INTRODUCTION

Recent studies robustly demonstrate the impact that parents exert upon children's chronic pain experience [11,22,37,52]. A burgeoning body of research has explored numerous facets of parental functioning and pain responses [16,18,34,44,49], including but not limited to parents' beliefs and worries about the child's pain [11,14], quality of the adolescent-parent relationship [31], and interactional patterns, e.g. the extent to which parents encourage their

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Conflicts of Interest: The authors have no conflicts of interest to disclose.

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child's adaptive or maladaptive pain responses [4,54]. Complex transactional processes appear to link children's and parents' emotional, cognitive, and behavioral responses to pain, ultimately influencing the child's overall functioning [6,39,43,52].

Parental cognitive responses to pain, such as parental pain catastrophizing or exaggerated negative pain appraisals, have received recent attention [12,13,17,48,50]. Goubert and colleagues [11] demonstrated that parent pain catastrophizing influences both parents' emotional reactions to pain and child functional disability. Recent work further clarifies these associations [3], supporting a mediational pathway from parental pain catastrophizing to parental emotional distress and ultimately to child disability. Parental pain catastrophizing may be an important precursor to more observable parental pain responses and eventually to child outcomes.

Behaviorally, parental protective responses to pain emerge as another key influence on child outcomes. Walker & Zeman [53] introduced the term "illness behavior encouragement" to describe parental protective responses to children's pain behavior, e.g. increasing attention to pain symptoms or excusing the child from responsibilities. Subsequent studies further illustrated how parental protective responses link to poorer functional outcomes, serving as the proximal link between parents' internal reactions (e.g. cognitions, emotional distress) and child outcomes [26,38,42,52]. These findings suggest a pathway from parental cognitions to parental behavioral pain responses to child functional outcomes.

To date, studies of parental responses to pain define child functional outcomes broadly, despite evidence that predictors of pain-related functioning vary across functional domains [9]. Although school impairment is a critical outcome in pediatric pain research [10,32,33,41], few studies focus specifically on this domain. This is a crucial outcome in pediatric pain, given evidence that long-term school impairment places individuals at heightened risk for poorer academic and occupational achievement [2], increased educational costs [8], and development of psychiatric disorders [2]. Studies that include school functioning outcomes [7,11,29] rely on school attendance as the sole indicator of this complex construct. Furthermore, studies have examined only isolated parental variables [7,11,29]. Additional studies must include multiple indicators of school functioning, test models incorporating multiple parent factors, and control for other known influences on pain-related school impairment such as child depressive symptoms [23,31,36].

The current study investigates associations between parental cognitive and behavioral responses to pain and school functioning in children with chronic pain, controlling for pain characteristics and child depressive symptoms. We sought to test whether parental behavioral responses to pain (i.e. protective behaviors) mediate associations between parental catastrophizing and school impairment). Specifically we hypothesized that a relation between parental pain catastrophizing and school functioning (assessed by multiple indicators) would be mediated by parental protective responses to pain, with greater parental pain catastrophizing associating with higher parental protectiveness, which in turn links to greater school impairment.

#### **METHODS**

#### **Participants**

All patients, ages 8–17, who underwent a multidisciplinary pain evaluation at a tertiary pain clinic in a large, urban northeast pediatric hospital between September 2008 and August 2010 were invited to participate along with their accompanying parent. Four hundred and one patients were approached and 350 agreed to participate, resulting in an 87% participation rate.

#### **Procedure**

Study measures were collected in the context of the child's multidisciplinary pain evaluation. Most measures (those assessing pain characteristics, school functioning, child depressive symptoms, and parental protective responses to pain) were administered as part of the standard clinical assessment. Measures of parents' cognitions related to the child's pain were completed separately as part of a larger IRB-approved research protocol [45]. Measures administered for clinical purposes were mailed to families prior to the child's evaluation; families were asked to complete those questionnaires independently and return them on the date of their appointment. If parents or children had not completed these questionnaires upon arrival to their appointment, they were asked to do so prior to the start of the evaluation. Pain ratings were obtained during the psychologist interview. At the clinic visit, eligible parents and children were approached by a research assistant prior to their evaluation. Additional measures were completed at this time, and consent/assent obtained for the use of data from the clinical assessment battery in addition to study-specific measures.

#### Measures

# Parental pain catastrophizing—The Pain Catastrophizing Scale for Parents (PCS-P)

[11] is a validated 13 item self-report measure of parents' negative thinking related to their child's chronic pain (e.g., "When my child is in pain, I can't keep it out of my mind.") The parent version of this measure is based on the widely used adult PCS [11] and has been shown to be psychometrically sound. Total scale scores are used in this study, with higher scores indicating greater levels of catastrophizing. The internal consistency for the total scores in this sample was .90.

## Parental protective responses to pain—The Adult Responses to Children's

**Symptoms** [5] scale assesses parents' responses to their children's pain in three subscales; parent protectiveness, minimization of pain, and encouraging and monitoring. For the present study, the 13-item protective responses subscale was used because it represents the pattern of parental pain response that is best supported theoretically and empirically [5,43]. The stem for each item is, "When your child has pain, how often do you ...?" Responses are rated on a 5-point scale ranging from "never" (0) to "always" (4), and subscale scores are computed by calculating the mean rating for items on each subscale. Higher scores indicate higher levels of parent protective responses. Examples include: "bring your child special treats or little gifts," and "Spend more time than usual with your child." The internal consistency for the protectiveness scale in this sample was .74.

#### **School functioning**

- 1. Attendance rates. Number of school days missed in the past three months due to pain (including for doctors' appointments) was obtained by parent report, which has been shown to correlate highly with official school attendance records [33]. Reports of days when the participant arrived to school late or left school early due to pain were incorporated into the count of missed days as half days missed. Raw responses were reduced into a six-point scale with categories representing 0 days missed, 1–5 days missed, 6–10 days missed, 11–20 days missed, 21–35 days missed, and greater than 35 days missed.
- 2. Global school functioning. The Pediatric Quality of Life Inventory (PedsQL) [47] school functioning subscale is a five-item measure of school functioning. Items all begin with the stem, "In the past one month, how much of a problem has your child had with..." and response options range from 0, "Never" to 4, "Almost Always." Example items are "Paying attention in class," and "Keeping up with

schoolwork." Raw scores are then transformed jnto standard scores on a 0–100 scale with higher score indicating better functioning (less impairment). Both parent- and child-report versions of the measure were included in the study, but child report was added after the study began, resulting in missing data. Given the high correlation between parent and child reports (r = 0.71, p<.001), parent report scores were used in data analyses. Cronbach's alpha for the five-item subscale was .86.

#### Other variables included in analyses

**Pain intensity**—Children provided pain intensity ratings for their average or usual pain using a 0–10 numeric rating scale, a reliable and valid method for obtaining children's self-report of pain in this age group [51].

**Time since pain onset**—Length of time since the initial onset of the current pain problem was measured in months based on parent report.

**Child depressive symptoms**—The **Children's Depression Inventory (CDI)** [24,25] is a well validated 27 item self-report measure of children's depressive symptoms that has been widely used in pediatric pain studies. It is a recommended outcome measure for clinical trials in pediatric chronic pain.

#### Data analysis

Descriptive statistics were used to characterize the sample and to check that all data met assumptions for use of parametric statistical tests. Bivariate Pearson r correlations were computed among all variables, including potentially relevant demographic variables, to inform the development of multivariate models. Hierarchical linear regression models were developed, with separate models tested for each of the two school functioning outcomes (school days missed and PedsQL school function scores). The extent to which parent protective responses mediated the relations between parent catastrophizing and child school functioning was examined with additional hierarchical multiple regression analyses. Bootstrapping as outlined by Preacher and Hayes [40] was done to test the indirect effects for both mediation models.

#### **RESULTS**

#### Participant characteristics

Child participants were primarily White (92.3%) and female (80.6%), consistent with the population of children with chronic pain seen in this tertiary care clinic setting. Mean age of children was 13.7 years (SD = 2.5). Primary pain diagnoses included neuropathic pain syndromes (e.g. Complex Regional Pain Syndrome; 34.3%), musculoskeletal pain (30.8%), back/neck pain (14.1%), chronic abdominal pain (8.9%), gynecological/genitourinary (5.8%), headache (2.0%) and other pain (e.g., chest, ear; 4.0%). Mothers were the participating parent in 90.5% of cases. Family socioeconomic status (SES) based on the four-factor index of social status [20] ranged from 12 to 66, with a mean of 45.5 (SD = 12.1). Regarding educational status, the majority of mothers (60%) and fathers (58%) had a college degree or above. Within the sample, 19.4% of responding parents reported themselves to be at home full time. The majority of responding parents (81%) were married.

#### Descriptive findings and preliminary analyses

Means and standard deviations for all variables included in analyses are reported in Table 1. Figure 1 depicts frequency of school absences across the sample. Results from bivariate

correlational analyses are shown in Table 2. T-tests revealed no differences in school outcomes based on race (White vs. other groups). Boys reported more school days missed than girls (boys' M=2.4, SD=1.9, girls' M=1.7, SD=1.7; F(317)=2.33, p<.05). Thus, gender was included as a covariate in regression equations testing effects of parental pain responses on school attendance. No gender differences were found on Peds-QL scores. Similarly, there were no gender differences in pain intensity, depression scores, parent pain catastrophizing or parental protective responses to pain. As expected, both pain intensity and depressive symptoms did correlate significantly with school function outcomes (See Table 2). Because time since pain onset did not correlate with any variables of interest, it was not included in subsequent multivariate analyses. A one-way ANOVA revealed no differences on predictor or outcome variable scores across pain diagnoses.

## Multivariate regression analyses

Four separate regression equations were tested to examine the effects of parental pain catastrophizing and parental protective responses to pain on school attendance rates and PedsQL school functioning scores. In each analysis, average pain intensity and child depressive symptoms measured on the CDI were entered on the first step of the equation to isolate the effects of the parent factors above and beyond the effects of pain and child depressive symptoms. Results of these four equations are summarized in Table 3. In each of the respective models, parent catastrophizing and protective parent behaviors were significant predictors of school outcomes above and beyond the impact of pain and child depressive symptoms.

To test our second hypothesis regarding a mediating effect of parental protective behaviors on the association between parental pain catastrophizing and school functioning, we conducted two hierarchical linear regression analyses, one for each school functioning outcome. Average pain intensity and child depressive symptoms were entered on the first step to control for these effects. Parental pain catastrophizing was entered on the second step as our independent variable, followed by parental protective behaviors on the final step of the equation as the hypothesized mediator. As described in Baron and Kenny (1986) [1] and Holmbeck (2002) [21], a decrease in the beta weight of the independent variable in the presence of the hypothesized mediator is evidence of a mediated effect. The results are detailed in Table 4. This significance of this effect was further tested using bootstrapping methods. The direct effect of parent catastrophizing on school attendance decreased from  $\beta$  = .14, p < .05 to  $\beta$  = .03, ns after the mediator, parent protectiveness, was entered into the regression equation. The Bootstrap test of the magnitude of this decrease was significant indicating that protectiveness mediated the relation between parent catastrophizing and child school attendance ( $\beta$  = .02, 95% CI .01, .03).

The direct effect of parent catastrophizing on PedsQL school functioning decreased from  $\beta$  = .20, p < .01 to  $\beta$  = .05, ns after the mediator, parent protectiveness, was entered into the regression equation. The Bootstrap test of the magnitude of this decrease was significant indicating that protectiveness mediated the relation between parent catastrophizing and PedsQl school functioning ( $\beta$  = -.34, 95% CI -.53, -.21). Finally, we explored a possible mediated effect by removing gender as a covariate and instead adding an interaction term (PCS x gender) to the analysis with school attendance as the outcome variable. However, child gender did not emerge as a statistically significant moderator of this mediational model.

#### DISCUSSION

This study examined effects of parental cognitive and behavioral responses to pain, specifically parental pain catastrophizing and parental protective behaviors, on school

functioning in a clinical sample of children experiencing chronic pain. We sought to test a mediational model wherein the effect of parental pain catastrophizing on school impairment was mediated by parental protective responses to the child's pain. The results support this hypothesis. Examined separately, parental pain catastrophizing and parental protective responses to child pain each predict school functioning outcomes, both in terms of school attendance rates and more global impressions of overall school functioning. Parent cognitive and behavioral responses to the child's pain account for significant unique variance in child school functioning above and beyond what is explained by the child's pain intensity and child depressive symptoms. Testing the proposed mediational pathway indicated that parental pain catrastrophizing exerts an indirect effect on the child's pain.

The view that parental responses to the child's pain influence school attendance and overall school impairment is consistent with the social learning theory framework that is often invoked to explain functional outcomes of pediatric chronic pain. This framework suggests that when certain illness behaviors or pain responses receive social rewards (e.g. increased expressions of parental support or concern, more time with parents), these behavior patterns are maintained and strengthened. Parents who have strong negative thoughts about pain and are extremely protective of their child in pain may be quick to sympathize with pain complaints and to acquiesce to requests to remain home from school due to pain. This pattern may be further reinforced if school absence is experienced as an avoidance of a negative or uncomfortable situation (i.e. being in school with pain). Catastrophizing and protective parents may also be more likely to interpret teachers' or schools' responses to their child's condition as unsympathetic, overly demanding, or disbelieving. Social learning influences on child pain behaviors have been shown to continue to predict pain responses into adulthood [28]. These long term effects underscore the importance of intervening early to help parents respond to children's pain in ways that encourage adaptive functioning, particularly in the school context where impairment exerts high and sometimes irreversible costs in terms of academic and social development.

The findings of the present study are consistent with other recent studies examining the role of parental responses to children in pain. Goubert (2006) [11] and others [3,42] have expanded our understanding of the chain of influence and the links between parent and child responses to pain, emphasizing that parental emotional distress over the child's pain shapes parents' pain-related thoughts and behaviors as well as child responses and functional outcomes. Their work points to the need to respond to parent distress as part of efforts to help parents develop more adaptive responses to child pain. Recent work by Vervoort and colleagues [50] supports a transactional pathway leading from child cognitive responses to pain, to parental behavioral responses to the child's pain, ultimately resulting in increases in child functional disability. These related models are not necessarily mutually exclusive; it is likely that there are multiple pathways that weave together child and parent responses to pain in various combinations, with further influences exerted by the larger family environment [30] as well as by other systems in which the child is embedded, such as school.

Previous studies have demonstrated associations between parental responses to pain and global functional disability [3,42] and one previous study has linked parental protective behaviors to school absence patterns in children with functional abdominal pain [29]. However, this is the first study to test a pathway from parental thoughts to parental behaviors and ultimately link these to school impairment. Furthermore, this study shows that the effects of parental responses to child's pain not only apply to school attendance but appear to influence school impairment more broadly, thus adding to the small but growing

literature aimed at improving our understanding of how childhood chronic pain impacts the school experience.

The findings of the study have clear clinical relevance. They underscore the importance of assessing parental and family factors in attempts to understand how chronic pain affects school functioning. Many parents who feel overwhelmed by their child's pain condition may be intimidated by the additional challenges of navigating complex school policies and procedures to advocate for their child's needs. In some cases, healthcare professionals can intervene in fairly simple ways to help deliver appropriate information to schools and ease parents' concerns about how their child is viewed and treated in the school setting. In line with recent studies suggesting that parental behaviors and distress are important targets to incorporate in interventions to improve pediatric pain-related functional disability [19,27], these results support the inclusion of parent factors as targets of cognitive-behavioral interventions specifically aimed at reducing school impairment among youth with chronic pain. It is important to note that in this study and previous studies by our group [33], children with chronic pain who are missing extensive amounts of school are a minority within the sample of children seeking care in the tertiary pediatric chronic pain clinic; however, they are an important subset of the clinical population because the extent of their school impairment has strong implications for their long-term functioning [2,8].

Several limitations to the study must be considered. First, parental participation was essentially limited to mothers. In light of several recent studies showing differences in both catastrophizing [17] and parental behavioral responses [50] between mothers and fathers and suggesting differential influences on child outcomes, future studies must examine the role of paternal influences on pain-related school impairment. There may also be differential effects by child gender and by specific parent-child dyads (e.g. mother-daughter vs. father-son, etc). However, the over-representation of girls in clinical chronic pain samples is a barrier to fully exploring possible gender effects. There were some limitations to the way in which school attendance data were collected. For example, days missed due to pain were not separated from days missed for doctors' appointments, and adjustments were not made to attendance rates to account for school vacation times potentially leading to some underestimation of the extent of school absence within the group. Future studies will continue to refine best approaches to collecting school attendance data. The cross-sectional design of the study limits our ability to draw clear conclusions about the causal direction of the relations tested. Although theory supports the assertion that parental cognitions give rise to parental behaviors and that these factors precede and predict child functional outcomes, longitudinal studies are necessary to provide stronger evidence of these claims. This study incorporated several parent factors in an effort to advance our understanding of the interplay among various parent influences on child functioning in the school context, but additional studies encompassing a broader array of parent and family factors and expanding beyond self-report measures of behavior are necessary to develop models comprehensive enough to adequately describe the complexity of family influences on the child pain experience.

This study gives rise to some intriguing directions for future research. The recent development of several validated assessment tools aimed at capturing a range of parental responses to pain, such as parental readiness to adopt a self-management approach to the child's pain [15], and parental psychological flexibility or pain acceptance [35,46] offer new avenues of inquiry to further clarify the impact of parental responses to child pain upon children's pain-related school impairment. Although the current study improves upon previous work by expanding the definition of school functioning beyond days absent, school functioning is a complex construct and the effects of chronic pain on school impairment are manifested in numerous, sometimes subtle, ways. Future studies will continue to expand our understanding of this multifaceted outcome domain in the context of pediatric pain.

Additionally, the influence of schools' and teachers' responses to children with chronic pain are not yet well understood and are an important focus of continued investigation. Merging these lines of inquiry, there may be salient aspects of the parent-school alliance, or lack thereof, that affect a child's ability to function with pain in school as well. Efforts to ensure that children succeed in the school environment despite pain must involve building strong collaborative relationships among healthcare providers, parents, and schools. Fostering such collaborations may at times be a challenging process but one that goes far toward promoting positive functional outcomes in children facing chronic pain.

## **Acknowledgments**

The study was supported by a Children's Hospital Boston Career Development Fellowship Award (LS), NIH grant K23HD067202 (LS), The Sara Page Mayo Endowment for Pediatric Pain Research and Treatment, and by the Department of Anesthesiology, Perioperative and Pain Medicine at Children's Hospital Boston. The authors also wish to thank Lisa Garcia, BA for her valuable research experience.

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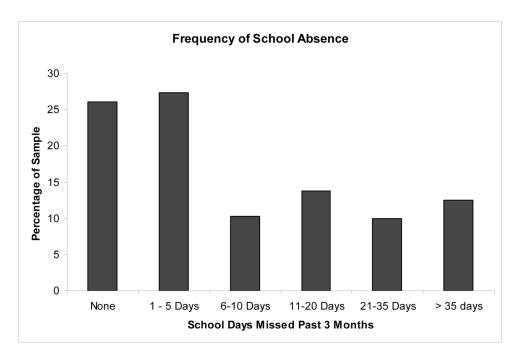
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**Figure 1.** Reported frequency rates of school absence in the past three months

Table 1

Means and Standard Deviations for Variables Variable ranges, means and standard deviations

Variable	Range	Mean (SD)
Time since pain onset (months)	1-206	24.1 (29.6)
Average pain rating	0-10	5.9 (2.1)
Child depression (CDI)	34-81	50.1 (10.7)
Parental pain catastrophizing (PCS-P)	5.0 - 52.0	26.6 (9.9)
Parental protective behavior (ARCS)	0 - 3.13	1.38 (.62)
School days missed (previous 3 months)	0 - 60	13.2 (17.7)
School functioning (PedsQL-School)	0-100	49.3 (23.9)

CDI = Childrens Depression Inventory; PCS-P = Pain Catastrophizing Scale; ARCS = Adult Responses to Children's Symptoms; PedsQL-School = Pediatric Quality of Life Inventory, School Function subscale.

Table 2

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Bivariate Pearson Correlation Matrix

Variable	Z	N 1 2	7	3	4	2	9	7	<b>∞</b>
1. Child age	319	1	.12*	.01	90.	90.	.00	80.	09
2. Time since pain onset	318		ı	14**02	02	05	01	01	02
3. Average pain rating	316			;	.22**	.17**	.17** .18**	.17**	23**
4. Depressive symptoms (CDI)	310				;	.28**	.27**	.27**	36**
5. Parent pain catastrophizing (PCS-P)	315					1	*14.	.22**	30**
6. Parent protective behavior (ARCS)	302						ı	.39**	54**
7. School days missed	319							1	59**
8. School functioning (PedsQL_School) 305	305	Ì							1

Correlations are two-tailed.

\*\* p<.01;

\* p<.05

CDI = Childrens Depression Inventory; PCS-P = Pain Catastrophizing Scale; ARCS = Adult Responses to Children's Symptoms; PedsQL-School = Pediatric Quality of Life Inventory, School Function subscale.

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 Table 3a

 Effects of parental catastrophizing and parent protectiveness on school absence

Variables	β	Beta	t	R <sup>2</sup> Change
Model I. (catastrophizing)				
Step 1				.12***
Child depression	.07	.28	5.00***	
Average pain rating	.10	.12	2.14*	
Child gender	.67	.16	2.88**	
Step 2				.02**
Child depression	.06	.24	4.25***	
Average pain rating	.09	.10	1.85	
Child gender	.65	.15	2.81**	
Pain catastrophizing	.02	.14	2.53*	
Model II. (protectiveness)				
Step 1				.12***
Child Depression	.07	.28	4.93***	
Average pain rating	.10	.12	2.11*	
Child gender	.67	.16	2.84**	
Step 2				.09***
Child depression	.05	.19	3.53***	
Average pain rating	.07	.08	1.53	
Child gender	.58	.13	2.54*	
Parental protectiveness	.87	.31	5.74***	

<sup>\*</sup>*P* < .05,

<sup>\*\*</sup>*P* < .01,

<sup>\*\*\*</sup> P<.001.

 Table 3b

 Effects of parental catastrophizing and protectiveness on PedsQL School Function scores

Variables	β	Beta	t	R <sup>2</sup> Change
Model I. (Catastrophizing)				
Step 1				.16***
Child depression	-1.13	34	-6.45***	
Average pain rating	-1.75	15	-2.88**	
Step 2				.04***
Child depression	97	29	-5.44***	
Average pain rating	-1.48	13	-2.48	
Pain catastrophizing	48	20	-3.76***	
Model II. (Protectiveness)				
Step 1				.16***
Child depression	-1.13	34	-6.43***	
Average pain rating	-1.75	15	-2.87**	
Step 2				.19***
Child depression	-7.37	22	-4.61***	
Average pain rating	-1.12	10	-2.08*	
Parental protectiveness	-17.86	46	-9.71***	

<sup>\*</sup>*P* < .05,

 $<sup>^{**}</sup>P < .01,$ 

<sup>\*\*\*</sup> P<.001.

Table 4a

Hierarchical linear regression model depicting the mediating effect of parent protective responses to pain on the relation between parent pain catastrophizing and child school attendance rates

Variables	β	Beta	t	R <sup>2</sup> Change
Step 1				.12***
Child depression	.07	.28	4.93***	
Average pain rating	.10	.12	2.11*	
Gender	.67	.16	2.84**	
Step 2				.02*
Child depression	.06	.24	4.19***	
Average pain rating	.09	.10	1.83	
Gender	.65	.15	2.77**	
Parent pain catastrophizing	.02	.14	2.49*	
Step 3				.07***
Child depression	.05	.19	3.36***	
Average pain rating	.07	.08	1.47	
Gender	.57	.13	2.53*	
Parent pain catastrophizing	.01	.04	0.67	
Parental protective responses	.83	.30	5.16***	

<sup>\*</sup>P < .05

<sup>\*\*</sup> P < .01

<sup>\*\*\*</sup> P<.001.

Table 4b

Hierarchical linear regression model depicting the mediating effect of parent protective responses to pain on the relation between parent pain catastrophizing and PedsQL school functioning scores.

Variables	β	Beta	t	R <sup>2</sup> Change
Step 1				.16***
Child depression	-1.13	34	-6.43***	
Average pain rating	-1.75	15	-2.9**	
Step 2				.04***
Child depression	97	29	-5.4***	
Average pain rating	-1.5	13	-2.5*	
Parent pain catastrophizing	-4.8	20	-3.7***	
Step 3				.16***
Child depression	71	21	-4.4***	
Average pain rating	-1.1	09	-2.0*	
Parent pain catastrophizing	12	05	88	
Parental protective responses	-17.2	45	-8.8***	

<sup>\*</sup>P < .05

 $<sup>^{**}</sup>P < .01,$ 

<sup>\*\*\*</sup> P<.001.