ARTICLE IN PRESS



RESEARCH
EDUCATION
TREATMENT
ADVOCACY



The Journal of Pain, Vol 00, No 00 (), 2019: pp 1–9 Available online at www.jpain.org and www.sciencedirect.com

Original Reports

Adverse Childhood Experiences in Mothers With Chronic Pain and Intergenerational Impact on Children

Catlin H. Dennis,* Denae S. Clohessy,*,† Amanda L. Stone,* Beth D. Darnall,‡ and Anna C. Wilson*

Abstract: Adverse childhood experiences (ACEs; eg, parental divorce, physical or sexual abuse) are more prevalent in individuals with chronic pain compared with the general population. Both increased maternal ACEs and chronic pain have been associated with poor physical and emotional functioning in offspring. However, the mechanisms driving these associations are poorly understood. Thus, this cross-sectional study evaluated the relation between maternal ACEs, mothers' current functioning, and children's physical and emotional functioning in a sample of mothers with chronic pain and their 8- to 12-year-old children. Results indicated a higher prevalence of ≥1 ACE in this sample of mothers with chronic pain (84%) compared with normative data from a community sample of women. Higher maternal ACE scores corresponded with lower physical and social functioning, greater anxiety and depressive symptoms, greater fatigue and sleep disturbances, and greater pain intensity and pain interference in mothers. Higher maternal ACE scores significantly correlated with higher child self-reported depressive symptoms, but not somatic symptoms or functional impairment. A path model indicated that maternal depressive symptoms accounted for the relation between higher maternal ACE scores and children's depressive symptoms. Intervening on maternal depression among mothers with chronic pain may reduce the impact of intergenerational ACE transmission.

Perspective: This article presents evidence regarding the intergenerational impact of ACEs in a large sample of mothers with chronic pain and their school-aged children. Maternal depressive symptoms accounted for the relation between maternal ACEs and children's depressive symptoms providing evidence regarding targets for preventive interventions.

© 2019 by the American Pain Society

Key words: Chronic pain, pediatric pain, adverse childhood experiences, ACEs, depression.

xposure to adverse childhood experiences (ACEs; eg, abuse, neglect, parental divorce) has been linked to a number of poor physical and mental health outcomes in adulthood. These poor health outcomes often include multiple somatic symptoms, chronic pain, depression and anxiety. In a study examining ACE prevalence in childhood and the risk of frequent headaches in

adulthood, researchers found that, as ACE scores increased, the prevalence and risk of headaches increased significantly. Individuals diagnosed with fibromyalgia are more likely to report experiencing ACEs than the general population³³ and, among adults with headaches, ACEs are associated with overlapping chronic pain conditions, ⁴² chronic versus episodic migraine, ⁴¹ and comorbid

Received September 7, 2018; Revised March 1, 2019; Accepted April 15, 2019.

Supported by the National Institutes of Health (NIH), Eunice Kennedy Shriver National Institute of Child Health and Human Development (R01 HD082200; PI Wilson), as well as by CTSA awards UL1TR000128/UL1TR002369. A.L.S. is supported by award numbers TL1TR002371 and T32GM108554 from NIH. D.S.C. is supported by the NIH Common Fund and Office of Scientific Workforce Diversity under three awards UL1GM118964, RL5GM118963, and TL4GM118965, administered by the National Institute of General Medical Sciences. The content is solely the responsibility of the authors and does not necessarily represent the

official views of the NIH. The authors have no conflicts of interest to

Supplementary data accompanying this article are available online at www.jpain.org and www.sciencedirect.com.

Address reprint requests to Catlin Dennis, Department of Pediatrics, Oregon Health & Science University, 707 SW Gaines Street, Portland, OR 97239. E-mail: dennica@ohsu.edu

1526-5900/\$36.00

© 2019 by the American Pain Society https://doi.org/10.1016/j.jpain.2019.04.004

^{*}Department of Pediatrics, Institute on Development and Disability, Oregon Health & Science University, Portland, Oregon, †Department of Psychology, Portland State University, Portland, Oregon, †Department of Anesthesiology, Perioperative and Pain Medicine, Stanford University School of Medicine, Stanford, California

2 The Journal of Pain

Intergenerational Impact of Mother's Adverse Childhood Experiences

anxiety and depressive symptoms.⁴⁰ Further, women experience higher levels of ACEs than men with approximately 15% of women experiencing ≥4 ACEs compared with 9% of men.³⁵ Thus, the relation between ACEs and chronic pain symptoms may be particularly important to evaluate in females.

Maternal ACEs and chronic pain have both been associated with poor physical and emotional health in children.^{29,39} A recent study found maternal ACEs were significantly associated with their children's developmental risk and that maternal depressive symptoms may be a potential mediator of this relationship.³⁹ Additional work has demonstrated that there is an intergenerational transmission of maternal adversity on infant socioemotional symptoms via adult maternal emotional outcomes (specifically depressive symptoms).²⁹ Similarly, children of mothers with chronic pain are at increased risk for poor emotional and physical functioning. 16 A recently developed integrative conceptual model proposed potential mechanisms through which the risk for chronic pain may be intergenerationally conferred, including social learning, parenting, and stressful environments.³⁸ Although the present article focuses on baseline data, the larger study that these data were derived from examines intergenerational pain transmission over 3 years. A history of ACEs in mothers with chronic pain could impact a number of these proposed mechanisms. For example, mothers who have experienced more ACEs are more likely to experience depression or posttraumatic stress symptoms, which may lead to difficulties with parenting and fostering secure attachments with their children. Although the impact of maternal ACEs has not been examined in offspring of parents with chronic pain, the increased rates of trauma in adults with chronic pain relative to the general population suggests that ACEs in mothers with chronic pain and their potential impact on children may be important to evaluate.²⁰

This study first aimed to evaluate the prevalence of ACEs in a large sample of mothers with chronic pain who have school-aged children. We expected a higher number of total ACEs in our sample relative to published rates of ACEs for women in the general population. Second, we aimed to examine the relation between maternal ACEs and mothers' own physical and emotional functioning, hypothesizing that a higher number of maternal ACEs would be associated with lower physical functioning and greater psychological symptoms. Third, we evaluated the association between maternal ACEs and children's pain, somatic symptoms, physical function, and depressive symptoms. We hypothesized that children of mothers who reported more ACEs would report greater pain frequency, somatic symptoms, functional impairment, and depressive symptoms. Finally, the present study evaluated 2 models to examine potential mechanisms which may account for the association between maternal ACEs and children's symptoms: 1) whether maternal physical functioning accounts for the association between maternal ACEs and children's functional impairment and 2) whether maternal depressive symptoms account for the association between maternal ACEs and children's depressive symptoms. We hypothesized that mothers with more ACEs would experience greater depressive symptoms and have poorer physical functioning,

which would account for greater depressive symptoms and greater functional impairment in their children.

Methods

Participants

Mothers with chronic pain and their children (n = 326 dyads) were recruited as a part of a longitudinal, observational, multisite study evaluating the impact of maternal chronic pain on children's emotional and physical functioning as they transition from childhood to adolescence. The present study used baseline data collected between August 16, 2016, and March 22, 2018; reported results are cross-sectional. Eligibility criteria for mothers included a) the presence of a current chronic pain condition for the past ≥6 months, b) pain occurring at least weekly, c) seeking specialty medical care for chronic pain within the past 6 months, d) living in the same home as the participating biological child ≥50% of the time, and e) the ability to complete online questionnaires in English. Children were eligible to participate in the present study if they were 8-12 years old at the start of participation and had the cognitive and English language abilities to complete online questionnaires. Children were enrolled between the ages of 8 and 12 to capture pain experiences during the transition to adolescence over a 3-year period of development. By the end of the study, child participants will be 11-15 years of age, a period of development when the incidence of chronic pain increases. Exclusion criteria for both mothers and children included a) current pain attributable to a lifethreatening or chronic illness (eg, cancer or diabetes) and b) a psychiatric hospitalization within the past 6 months.

Procedures

Mothers were recruited from tertiary referral pain clinics at 3 major academic medical centers in the Western United States, research databases (eg, ResearchMatch) and through online advertisements on social media (eg, Facebook, Twitter). The institutional review board at each academic medical center where participant recruitment occurred approved the study protocol. Mothers first completed an initial contact form indicating interest in receiving more information about the study. Once received by the study team, a trained research assistant spoke with each interested individual over the phone to provide further information regarding the study, screen for eligibility, and review the informed consent and assent forms. After consent, dyads were enrolled in the study and completed all study questionnaires through Research Electronic Data Capture (REDCap), a secure online data collection site.¹³ Mothers were specifically instructed to have their child complete the questionnaires independently and only provide assistance with unfamiliar words to reduce bias. After completing all study procedures for the baseline time point, the mother and child were each compensated with a \$30 electronic gift card to an online retailer; compensation increased by \$10 each year that the family continued to participate.

Measures

Parent Measures

ACEs questionnaire. The ACE questionnaire was designed to assess ten categories of childhood trauma that occurred before an individual's 18th birthday. These categories include 1) emotional, 2) physical, or 3) sexual abuse; 4) lack of emotional support; 5) basic needs unmet; 6) parental separation or divorce; 7) violence against female relatives; or 8) living with household members who were substance abusers, 9) mentally ill, or 10) imprisoned. 12

Maternal pain characteristics

Mothers completed a questionnaire regarding their current pain problem and chronic pain history. Current pain locations were assessed with a body map in REDCap. Generalized pain was calculated with criteria commonly used for diagnosing fibromyalgia by computing sum scores for each of the 5 body regions (left upper, right upper, axial, left lower, right lower). ⁴⁵ If 4 of the 5 regions were reported as having pain on the Widespread Pain Index body map, then the participant met the criteria for generalized pain. Jaw, chest, and abdominal pain were not included in the definition of generalized pain. In addition to current pain characteristics, mothers also reported the age of onset. Mothers who reported a pain onset before age 18 were considered to have childhood-onset chronic pain.

Patient-Reported Outcomes Measurement Information System-29 Profile v.2.0. Mothers completed the Patient-Reported Outcomes Measurement Information System (PROMIS)-29 Profile, 15 which assesses general emotional health and physical functioning throughout 7 domains (4 questions each). The domains include pain interference, physical functioning, anxiety, depression, fatigue, sleep disturbance, and ability to participate in social roles and activities. For each PROMIS domain, the prorated total raw score is computed using the number of items completed and is then converted to T-scores. For each of the domains, excluding ability to participate in social roles and activities and sleep disturbance, a T-score of 50 is representative of the average United States population. Ability to participate in social roles and activities and sleep disturbance were enhanced for chronic illness and represent a calibration sample rather than the general United States population. An 8th domain, pain intensity, is rated on a numeric rating scale ranging from 0 (not at all) to 10 (worst pain imaginable) and is not converted to a T-score during the scoring process.⁴ In the present study, all 7 domains exhibited high internal consistency (Cronbach's α range = .83–.94).

Child Measures

Child pain frequency. Children reported on their own pain frequency using a survey question asking, "In the past 3 months how often have you had aches or pains?" Response options range from 0 (not at all) to 6 (daily).

PROMIS Pediatric Depressive Symptoms Short Form. Children completed the PROMIS pediatric depressive symptoms short form (8 items). ¹⁹ This measure assesses depressive symptoms in pediatric samples, aged 8–17 years and was developed through the use of the PROMIS pediatric item banks. It is not meant to be a diagnostic test for depression, but for general depressive symptoms. Similar to the adult PROMIS profile, this measures depressive symptoms over a 7-day period rated on a 5-point scale from 0 (never) to 4 (almost always). The summed scores are scaled based on a T-score of 50, the same for the adult PROMIS profile. The 8-item short form showed a reliability coefficient of .85 in the current sample.

Functional Disability Inventory. Children completed the Functional Disability Inventory (FDI). 44 The FDI measured the extent to which children would have had trouble completing activities owing to their health over the past 2 weeks. Examples of items assessed include difficulty walking upstairs, being at school all day, watching television, and getting to sleep and staying asleep. Children were asked to rate their difficulties on a 0 (no trouble) to 4 (impossible) scale. The FDI includes 15 items, yielding total scores ranging from 0 to 60. Higher scores indicate greater functional impairment. The alpha reliability for the FDI in this sample was .92.

Children Somatic Symptoms Inventory. Children completed the 24-question Children Somatic Symptoms Inventory to assess children's somatic symptoms (eg, headaches, weakness in body, nausea, etc.). 43,44 Children were asked to rate how much they were bothered by each symptom in the past 2 weeks on a 5-point scale from 0 (not at all) to 4 (a whole lot). Total scores range from 0 to 96 and were computed by summing the items. Higher scores indicate greater somatic symptom distress. The alpha reliability for the Children Somatic Symptoms Inventory-24 in this sample was .91.

Data Analyses

Data analyses were completed using SPSS version 24 (SPSS, College Station, Texas). First, descriptive statistics were conducted for the ACEs measure to examine the prevalence and distribution of the number of ACEs reported in the current sample. We conducted a χ^2 test to compare the proportion of mothers reporting ≥ 1 ACE in our sample to normative data for women in the United States provided by the Centers for Disease Control and Prevention (CDC)-Kaiser ACE Study. 5 Next, independent samples t-tests evaluated differences in ACE scores between mothers with particular pain characteristics (generalized vs localized, childhood onset vs adult onset). The total number of ACEs were correlated with PROMIS domains using Pearson r correlations to evaluate the relation between ACE scores and mothers' current symptoms and functioning. Owing to the number of maternal domains assessed, the alpha level was set at .001 for correlations between maternal ACEs and their own symptoms and functioning. Pearson r correlations also evaluated the relation between maternal ACE

DEMOGRAPHIC VARIABLE

4 The Journal of Pain

scores and children's depressive symptoms, somatic symptoms, and functional impairment. Spearman's rho evaluated the relation between maternal ACEs and children's pain frequency owing to its ordinal nature. For correlations with child self-reported symptoms and functioning, the alpha level was set a .05. Finally, mediation analyses were conducted using the PROCESS Macro for SPSS.¹⁴ The indirect effect was tested using a bootstrap estimation approach with 5000 samples. With this approach, the indirect effect is considered statistically significant if the 95% confidence interval does not cross 0. Based on Monte Carlo simulations, mediation analyses were adequately powered (β = .81) to detect a small effect (.20) for the indirect pathway with a sample size of 326. A small proportion of dyads were missing data for one of the key variables for the path analyses (n = 2).6%) and were excluded from analyses given that these

Results

Demographics and Pain Characteristics

data were considered missing at random.

Table 1 provides a summary of demographic characteristics. The sample is comprised of mothers who were on average 40.3 years old (SD = 5.85; range = 24.49–54.31), predominately Caucasian, and married. Children were on average 9.89 years old (SD = 1.39), predominately Caucasian, and female. The majority of mothers reported adult-onset chronic pain (\geq 18 years of age; 73.9%, n = 241), with about one-fourth reporting childhoodonset chronic pain (26.1%, n = 85). Mothers reported an average pain intensity of 5.04 (SD = 1.62) on a 0 to 10 numeric rating scale. Nearly one-half of the mothers met criteria for generalized pain based on their self-reported pain locations (45.7%, n = 149).

Distribution of ACEs in Mothers With Chronic Pain

On average, mothers reported 3.42 of 10 possible ACEs (see Figure 1 for the distribution and Table 2 for the frequency of ACEs). A small proportion of the sample (16.0%, n = 52) reported never experiencing an ACE; thus, a significant majority of the sample experienced ≥ 1 ACE (84.0%, n = 274). Results from a χ^2 test comparing the proportion of women who experienced ≥ 1 ACE in our sample to women in the original CDC-Kaiser ACE Study⁵ indicated that mothers with chronic pain in our sample were significantly more likely to endorse ≥1 ACE compared with a sample of women recruited from the general population (65.5%; difference = 18.5%, 95% CI = 14.02–22.21%, $\chi^2(1)$ = 48.13, P < .001). Further, mothers with chronic pain in our sample were significantly more likely to endorse ≥4 ACEs (44.5%) compared with the sample of women from the CDC-Kaiser ACE Study (15.2%, difference = 29.3%, 95% CI = 23.95-34.77, $\chi^2(1) = 199.35, P < .001).^5$

Mothers most frequently endorsed the following ACEs: a) mental illness in household, b) parental separation or divorce, c) emotional abuse, d) emotional neglect, and e)

Intergenerational Impact of Mother's Adverse Childhood Experiences

Table 1. Demographic Characteristics (N = 326)

Mother	
Maternal age, y	40.30 ± 5.85
Marital status	
Married	77.6 (253)
Divorced or separated	16.9 (55)
Never married	5.5 (18)
Employment status	
Employed, full or part time	47.2 (154)
Not currently working	33.4 (109)
Receiving disability	18.4 (60)
Annual household income	
≤\$25,000	22.7 (38)
\$25,001-\$49,999	21.5 (70)
\$50,000-\$79,999	17.8 (58)
\$80,000-\$119,999	27.9 (91)
≥\$120,000	17.8 (58)
Race	
Caucasian	89.9 (293)
Minority racial group (Asian, Black,	5.2 (17)
American Indian, other)	
Biracial or multiple races	4.9 (16)
Ethnicity, Hispanic	6.7 (22)
Generalized pain	45.7 (149)
Years since chronic pain onset	15.81 ± 9.92
Child	
Child age, y	9.89 ± 1.39
Child sex	
Female	52.1 (170)
Male	47.9 (156)
Child race	
Caucasian	83.1 (271)
Minority racial group (Asian, Black, American Indian, other)	4.9 (16)
Biracial or multiple races	12.0 (39)
Child ethnicity, Hispanic	12.3 (40)
Child pain frequency, past 3 months	
None	11.5 (57)
<1 time per month	15.3 (50)
1–3 times per month	26.1 (85)
About 1 time per week	16.3 (53)
2–3 times per week	11.3 (37)
4–6 times per week	6.1 (20)
Daily	7.1 (23)

Values are mean \pm standard deviation or percent (n).

household substance abuse. Sexual abuse and physical abuse were each reported by approximately one-third of the sample (interpersonal violence was determined by a positive answer to either item 2 or item 3) with nearly one-half of the sample (47.9%, n = 156) reporting either form of interpersonal violence. Physical neglect, observing their mother being treated violently, and a house-hold member in prison were less frequently endorsed.

Relation of ACEs to Maternal Pain Characteristics

Mothers with childhood-onset chronic pain, compared with mothers with adult-onset chronic pain, reported significantly more ACEs (t[324] = -2.49, P = .013;

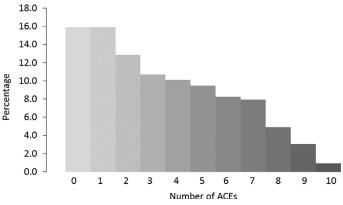


Figure 1. Distribution of ACEs in mothers with chronic pain.

childhood onset: mean = 4.05, adult onset: mean = 3.20). Mothers with generalized pain, compared with those without, reported slightly more ACEs (mean = 3.72 vs mean = 3.17), but this difference did not reach statistical significance (t[299] = -1.83, P = .07). Table 3 presents the correlations between maternal ACE scores and domains of physical and emotional functioning from the

PROMIS-29. Although statistically significant, all correlation coefficients between ACE scores and other variables were small. Higher maternal ACE scores corresponded with lower physical and social functioning, greater anxiety and depressive symptoms, greater fatigue and sleep disturbances, and greater pain intensity and pain interference in mothers.

Table 2. Frequency of ACEs in Mothers With Chronic Pain

Types and Frequencies of Maternal ACEs reported*	Percent (n)
ACE Q9: Mental illness in household	54.0 (176)
ACE Q6: Parental separation or divorce	50.0 (163)
ACE Q1: Emotional abuse	47.9 (156)
ACE Q4: Emotional neglect	44.8 (146)
ACE Q8: Household substance abuse	40.2 (131)
ACE Q3: Sexual abuse	34.7 (113)
ACE Q2: Physical abuse	30.1 (98)
ACE Q5: Physical neglect	16.6 (54)
ACE Q7: Observation of mother/stepmother	16.3 (53)
being treated violently	
ACE Q10: Household member in prison	8.0 (26)
Total ACEs endorsed, mean \pm standard deviation	3.42 ± 2.71

NOTE: ACE Q# refers to the question number on the ACE questionnaire. *n = 326.

Relation of Maternal ACEs to Children's Physical and Emotional Functioning

Table 4 presents the correlations between maternal ACE scores and child emotional and physical functioning. Higher maternal ACE scores significantly correlated with higher child self-reported depressive symptoms (r = .14, P = .02), but not pain frequency (r = .08), somatic symptoms (r = .02), or functional impairment (r = .03). Owing to the lack of relation between maternal ACEs and children's pain, somatic symptoms, and functional impairment, further analyses focus exclusively on children's depressive symptoms (Figure 2).

We tested a path model to evaluate the direct and indirect associations between maternal ACEs and children's depressive symptoms via mother's own depressive symptoms. Higher maternal ACE scores were associated with greater maternal depressive symptoms (α path,

Table 3. Correlations Between Maternal ACE Scores and Mother's Own Symptoms and Functioning Measured by the PROMIS-29 Profile

	MATERNAL ACEs	PAIN INTENSITY	PAIN Interference	ANXIETY	DEPRESSIVE SYMPTOMS	FATIGUE	SLEEP DISTURBANCE	PHYSICAL FUNCTIONING	FUNCTIONING IN SOCIAL ROLES
Maternal ACEs									
Pain intensity	.15								
Pain interference	.19*	.57*							
Anxiety	.23*	.29*	.39*						
Depressive symptoms	.18*	.30*	.44*	.71*					
Fatigue	.23*	.35*	.57*	.46*	.49*				
Sleep disturbance	.22*	.33*	.44*	.37*	.39*	.52*			
Physical functioning	19*	43*	58*	27*	37*	44*	40*		
Functioning in social roles	20*	36*	68*	29*	38*	58*	36*	.59*	
Mean	3.42	5.91	65.01	59.22	56.52	64.17	57.99	39.29	39.93
SD	2.71	1.65	6.25	8.31	8.73	8.20	7.69	6.67	6.76

6 The Journal of Pain

Intergenerational Impact of Mother's Adverse Childhood Experiences

Table 4. Correlations Between Maternal ACE Scores and Child Symptoms and Functioning

	MATERNAL ACES	PAIN FREQUENCY	DEPRESSIVE SYMPTOMS	SOMATIC SYMPTOMS	FUNCTIONAL IMPAIRMENT
Maternal ACEs					
Pain frequency	.08				
Depressive symptoms	.14*	.21*			
Somatic symptoms	.02	.53*	.48*		
Functional impairment	.03	.34*	.40*	.59*	
Mean			48.45	14.34	7.10
SD			9.47	12.59	9.08

NOTE: Correlations with pain frequency are Spearman's rho. See Table 1 for pain frequency descriptive statistics. *P < .05.

b = .27, 95% CI = .12–.42, P < .001), and greater maternal depressive symptoms were associated with greater child depressive symptoms (β path, b = .32, 95% CI = .15 – .50, P < .001). Higher maternal ACE scores were associated with greater child depressive symptoms (c path, b = .26, 95% CI = .01–.51, P = .04), but with the inclusion of maternal depressive symptoms, the relation between maternal ACE scores and child depressive symptoms (c' path, b = .17, 95% CI = -.08–.42, P = .17) was no longer significant. The indirect path for the relation between maternal ACE scores and child depressive symptoms via maternal depressive symptoms was significant ($\alpha\beta$ = .09, bootstrapped 95% CI = .03–.17, P = .01).

Discussion

The experience of multiple ACEs can have lasting adverse effects into adulthood and have been associated with a number of poor health outcomes, including chronic pain. 18,20 Consistent with this literature, our study found that mothers with chronic pain reported experiencing significantly more ACEs compared with women in the general population. Furthermore, a higher number of maternal ACEs significantly corresponded with greater maternal pain interference, anxiety, depressive symptoms, fatigue, sleep disturbance, and lower physical and social functioning. Both maternal chronic pain and ACEs could have an intergenerational impact on offspring, 38,46 potentially contributing to the perpetuation of a high level of disease burden

for some families. We found a significant association between a higher number of maternal ACEs and child depressive symptoms, but not child pain frequency, somatic symptoms, or functional impairment. Results from a path model indicated that, for mothers with chronic pain, the intergenerational association between maternal ACEs and children's psychological functioning may be accounted for by the mother's depressive symptoms. Other studies suggest similar models for ACE transmission between generations.^{25,30} Thus, the intergenerational impact of maternal ACEs on their child's psychological functioning may be mitigated through preventive interventions focused on maternal depressive symptoms as well as supportive interventions for parenting within the context of challenging health conditions.

As hypothesized, mothers in the current study reported a high number of ACEs compared with women in the general population. The CDC reports that 65.5% of U.S. women report ≥1 ACE, and that 84% of this chronic pain sample reports ≥1 ACE, demonstrating a significant difference between groups.³⁵ The occurrence of many ACEs in childhood could result in alterations in physiological processes such as hypothalamic—pituitary—adrenal axis functioning,² neuronal plasticity,⁶ and epigenetic regulation,²² which contribute to the development of chronic pain or exacerbation of other pain complaints; some ACEs may also result in physical injuries that could contribute to the development of chronic pain.

In the current study, a dose-response relationship was observed among ACEs such that, as ACEs increased,

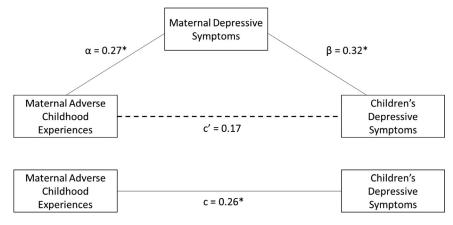


Figure 2. Direct and indirect effects of maternal ACEs on children's depressive symptoms in mothers with chronic pain. *Paths significant at the P < .05 level.

physical and social functioning declined and anxiety and depressive symptoms increased, as did reports of fatigue, sleep disturbances, pain intensity, and pain interference. These findings align with other literature suggesting that ACEs significantly impact the occurrence and persistence of pain in adulthood. Por instance, 1 chronic pain study found that individuals who reported greater tender point counts were significantly more likely to report ACEs.

Mothers with childhood-onset chronic pain reported experiencing more ACEs compared with mothers with adult-onset chronic pain, suggesting that ACEs may contribute to the development of pediatric chronic pain, which then persists into adulthood; ACEs have indeed been associated with pediatric chronic pain. ACEs were approximately 20% more likely to be diagnosed with a chronic pain condition in their childhood. Adverse experiences in childhood leave a lasting imprint during critical pediatric developmental periods and seem to alter the trajectory of physical and mental health into adulthood, which can extend into the next generation. ACEs were

Contrary to one of our hypotheses, maternal ACEs were not significantly related to children's somatic symptoms or functional impairment. The current study presents only baseline data from a longitudinal study; all children included in this study denied having any severe illness and were intentionally recruited before the onset of adolescence when the incidence of chronic pain substantially increases and, thus, represent a generally healthy, but at-risk sample. As the study progresses, it is possible that longitudinal follow-up will show a relationship between maternal ACEs and trajectories of children's pain, somatic symptoms, or disability that was not observed in baseline analyses. There is some evidence that children's depressive symptoms increase risk for the development of pain problems 11,37 and, thus, following these children longitudinally could provide greater insight into indirect pathways through which maternal ACEs and chronic pain may impact the development of chronic pain in youth. Although certain pain conditions have a strong genetic component, research indicates that children of parents with chronic pain are at increased risk of developing a chronic pain condition in adulthood beyond any genetic contributions.8,17,38 General parenting, family health, and exposure to a stressful environment may play key roles in explaining why children of parents with chronic pain may be at risk for developing chronic pain and poorer psychological outcomes in their adult lives.

Further, it is important to consider the cumulative impact ACEs, current depressive symptoms, and chronic pain could have on parenting. Indeed, research has revealed that, among women with chronic pain who have dependents living with them, pain, guilt, and anxiety about how their pain negatively impacts their parent—child relationships is substantial.⁴⁷ Additionally, these same women report having difficulty prioritizing appropriate self-care owing to the competing interests of caregiving for others. Future research is needed to further understand how specific supports and

interventions might help to support parenting in the context of chronic pain. Furthermore, future studies should examine the effects of paternal ACEs on parent, child, and family functioning.

Our results should be interpreted in light of a number of limitations. The results presented are cross-sectional; therefore, no temporal effects can be inferred. However, maternal ACEs are a retrospective report of events which occurred before the age of 18; thus, it can be inferred that these events preceded current depressive symptom severity. It is also important to note that although maternal ACEs preceded current maternal depressive symptoms, these symptoms may also stem from current stressors; the same may also be true for child depressive symptoms. Child depressive symptoms were, on average, not in the clinical range in this at-risk sample; however, subclinical levels of depressive symptoms are known to impact child and adolescent social development and increase risk for major depressive disorder in adulthood.^{21,34}

Participants were instructed verbally by study staff during the consent process and in both the parent consent form and the child assent form to have the child complete their study materials independently; however, we cannot definitively guarantee that every child report was completed independently by the child. Additionally, although the ACE questionnaire has been well-validated, there is the possibility that, given the nature of the questions, participants may have underreported or inaccurately reported on these items.^{3,31} Children in this study were enrolled when they were between the ages of 8 and 12 years old; therefore, these findings may not be generalizable to other age ranges as research suggests that stress effects have a unique impact depending on the developmental period in which they are experienced.²⁶ Last, this study's sample seems to have slightly higher educational attainment on average, compared with general population samples in other studies 10,35; this sociodemographic feature, or others specific to the current sample, may limit the generalizability of results.

Despite these limitations, the current study has several strengths, namely, the large number of participants, and the dyadic design—comprised of mothers and their biological children—that allowed for examination of symptoms across generations. Further, the focus on possible mechanisms accounting for the relation between maternal ACEs and children's symptoms is a strength as ACEs in and of themselves likely do not exert a direct path in intergenerational transmission of risk. Given both a high number of maternal ACEs and the presence of maternal chronic pain have been associated with increased risk for adverse physical and psychological health outcomes in children, it is important to consider the potential additive effects of both a high ACE burden and chronic pain in mothers.

Supplementary data

Supplementary data related to this article can be found at https://doi.org/10.1016/j.jpain.2019.04.004.

ARTICLE IN PRESS

8 The Journal of Pain

References

- 1. Anda R, Tietjen G, Schulman E, Felitti V, Croft J: Adverse childhood experiences and frequent headaches in adults. Headache 50:1473-1481, 2010
- 2. Anda RF, Felitti VJ, Bremner JD, Walker JD, Whitfield C, Perry BD, Dube SR, Giles WH: The enduring effects of abuse and related adverse experiences in childhood. Eur Arch Psychiatry Clin Neurosci 256:174-186, 2006
- 3. Bethell CD, Carle A, Hudziak J, Gombojav N, Powers K, Wade R, Braveman P: Methods to assess adverse childhood experiences of children and families: Toward approaches to promote child well-being in policy and practice. Acad Pediatr 17:S51-S69, 2017
- 4. Cella D, Riley W, Stone A, Rothrock N, Reeve B, Yount S, Amtmann D, Bode R, Buysse D, Choi S, Cook K, DeVellis R, DeWalt D, Fries JF, Gershon R, Hahn EA, Lai J-S, Pilkonis P, Revicki D, Rose M, Weinfurt K, Hays R: Initial adult health item banks and first wave testing of the Patient-Reported Outcomes Measurement Information System (PROMIS(TM)) network: 2005–2008. J Clin Epidemiol 63:1179-1194, 2010
- **5.** Centers for Disease Control and Prevention: The ACE Study Survey Data. Atlanta, GA, U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, 2016
- **6.** Champagne DL, Bagot RC, van Hasselt F, Ramakers G, Meaney MJ, de Kloet ER, Joels M, Krugers H: Maternal care and hippocampal plasticity: Evidence for experience-dependent structural plasticity, altered synaptic functioning, and differential responsiveness to glucocorticoids and stress. J Neurosci 28:6037-6045, 2008
- 7. Chapman DP, Dube SR, Anda RF: Adverse childhood events as risk factors for negative mental health outcomes. Psychiatr Ann 37:359-364, 2007
- **8.** Craig TK, Cox AD, Klein K: Intergenerational transmission of somatization behaviour: A study of chronic somatizers and their children. Psychol Med 32:805-816, 2002
- **9.** Davis DA, Luecken LJ, Zautra AJ: Are reports of childhood abuse related to the experience of chronic pain in adulthood? A meta-analytic review of the literature. Clin J Pain 21:398-405, 2005
- 10. Dong M, Anda RF, Felitti VJ, Dube SR, Williamson DF, Thompson TJ, Loo CM, Giles WH: The interrelatedness of multiple forms of childhood abuse, neglect, and household dysfunction. Child Abuse Negl 28:771-784, 2004
- **11.** Dunn KM, Jordan KP, Mancl L, Drangsholt MT, Le Resche L: Trajectories of pain in adolescents: A prospective cohort study. Pain 152:66-73, 2011
- 12. Felitti VJ, Anda RF, Nordenberg D, Williamson DF, Spitz AM, Edwards V, Koss MP, Marks JS: Relationship of childhood abuse and household dysfunction to many of the leading causes of death in adults. The Adverse Childhood Experiences (ACE) Study. Am J Prev Med 14:245-258, 1998
- 13. Harris PA, Taylor R, Thielke R, Payne J, Gonzalez N, Conde JG: Research Electronic Data Capture (REDCap) A metadata-driven methodology and workflow process for providing translational research informatics support. J Biomed Inform 42:377-381, 2009

Intergenerational Impact of Mother's Adverse Childhood Experiences

- **14.** Hayes AF: Introduction to Mediation, Moderation, and Conditional Process Analysis: A Regression-Based Approach, 2nd ed. New York, NY, Guilford Press, 2013
- 15. Hays RD, Spritzer KL, Schalet BD, Cella D: PROMIS((R))-29 v2.0 profile physical and mental health summary scores. Qual Life Res 27:1885-1891, 2018
- **16.** Higgins KS, Birnie KA, Chambers CT, Wilson AC, Caes L, Clark AJ, Lynch M, Stinson J, Campbell-Yeo M: Offspring of parents with chronic pain: A systematic review and meta-analysis of pain, health, psychological, and family outcomes. Pain 156:2256-2266, 2015
- 17. Hoftun GB, Romundstad PR, Rygg M: Association of parental chronic pain with chronic pain in the adolescent and young adult: Family linkage data from the HUNT Study. JAMA Pediatr 167:61-69, 2013
- **18.** Hughes K, Bellis MA, Hardcastle KA, Sethi D, Butchart A, Mikton C, Jones L, Dunne MP: The effect of multiple adverse childhood experiences on health: A systematic review and meta-analysis. Lancet Public Health 2:e356-e366, 2017
- 19. Irwin DE, Stucky B, Langer MM, Thissen D, DeWitt EM, Lai J-S, Varni JW, Yeatts K, DeWalt DA: An item response analysis of the pediatric PROMIS anxiety and depressive symptoms scales. Qual Life Res 19:595-607, 2010
- **20.** Jones GT, Power C, Macfarlane GJ: Adverse events in childhood and chronic widespread pain in adult life: Results from the 1958 British Birth Cohort Study. Pain 143:92-96, 2009
- 21. Kochel KP, Ladd GW, Rudolph KD: Longitudinal associations among youth depressive symptoms, peer victimization, and low peer acceptance: An interpersonal process perspective. Child Dev 83:637-650, 2012
- **22.** Labonte B, Suderman M, Maussion G, Navaro L, Yerko V, Mahar I, Bureau A, Mechawar N, Szyf M, Meaney MJ, Turecki G: Genome-wide epigenetic regulation by early-life trauma. Arch Gen Psychiatry 69:722-731, 2012
- 23. Lampe A, Doering S, Rumpold G, Solder E, Krismer M, Kantner-Rumplmair W, Schubert C, Sollner W: Chronic pain syndromes and their relation to childhood abuse and stressful life events. J Psychosom Res 54:361-367, 2003
- 24. Larsson B, Sund AM: Emotional/behavioural, social correlates and one-year predictors of frequent pains among early adolescents: Influences of pain characteristics. Eur J Pain 11:57-65, 2007
- 25. Le-Scherban F, Wang X, Boyle-Steed KH, Pachter LM: Intergenerational associations of parent adverse childhood experiences and child health outcomes. Pediatrics 141, 2018
- **26.** Lupien SJ, McEwen BS, Gunnar MR, Heim C: Effects of stress throughout the lifespan on the brain, behaviour and cognition. Nat Rev Neurosci 10:434-445, 2009
- **27.** McBeth J, Macfarlane GJ, Benjamin S, Morris S, Silman AJ: The association between tender points, psychological distress, and adverse childhood experiences: A community-based study. Arthritis Rheum 42:1397-1404, 1999
- **28.** McCall-Hosenfeld J, Winter M, Heeren T, Liebschutz JM: The association of interpersonal trauma with somatic symptom severity in a primary care population with chronic

pain: Exploring the role of gender and the mental health sequelae of trauma. J Psychosom Res 77:196-204, 2014

- **29.** McDonnell CG, Valentino K: Intergenerational effects of childhood trauma: Evaluating pathways among maternal ACEs, perinatal depressive symptoms, and infant outcomes. Child Maltreatment 21:317-326, 2016
- **30.** Metzler M, Merrick MT, Klevens J, Ports KA, Ford DC: Adverse childhood experiences and life opportunities: Shifting the narrative. Child Youth Serv Rev 72:141-149, 2017
- **31.** Murphy A, Steele M, Dube SR, Bate J, Bonuck K, Meissner P, Goldman H, Steele H: Adverse Childhood Experiences (ACEs) questionnaire and Adult Attachment Interview (AAI): Implications for parent child relationships. Child Abuse Negl 38:224-233, 2014
- **32.** Nelson SM, Cunningham NR, Kashikar-Zuck S: A conceptual framework for understanding the role of adverse childhood experiences in pediatric chronic pain. Clin J Pain 33:264-270, 2017
- **33.** Olivieri P, Solitar B, Dubois M: Childhood risk factors for developing fibromyalgia. Open Access Rheumatol 4:109-114, 2012
- **34.** Pine DS, Cohen P, Gurley D, Brook J, Ma Y: The risk for early-adulthood anxiety and depressive disorders in adolescents with anxiety and depressive disorders. Arch Gen Psychiatry 55:56-64, 1998
- **35.** Centers for Disease Control and Prevention: The ACE Study Survey Data. Atlanta, GA, U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, 2016
- **36.** Sherman AL, Morris MC, Bruehl S, Westbrook TD, Walker LS: Heightened temporal summation of pain in patients with functional gastrointestinal disorders and history of trauma. Ann Behav Med 49:785-792, 2015
- **37.** Stahl M, Kautiainen H, El-Metwally A, Hakkinen A, Ylinen J, Salminen JJ, Mikkelsson M: Non-specific neck pain in schoolchildren: Prognosis and risk factors for occurrence and persistence. A 4-year follow-up study. Pain 137:316-322, 2008

38. Stone AL, Wilson AC: Transmission of risk from parents with chronic pain to offspring: An integrative conceptual model. Pain 157:2628-2639, 2016

- **39.** Sun J, Patel F, Rose-Jacobs R, Frank DA, Black MM, Chilton M: Mothers' adverse childhood experiences and their young children's development. Am J Prev Med 53:882-891, 2017
- **40.** Tietjen GE, Brandes JL, Peterlin BL, Eloff A, Dafer RM, Stein MR, Drexler E, Martin VT, Hutchinson S, Aurora SK: Childhood maltreatment and migraine (part I). Prevalence and adult revictimization: A multicenter headache clinic survey. Headache 50:20-31, 2010
- 41. Tietjen GE, Brandes JL, Peterlin BL, Eloff A, Dafer RM, Stein MR, Drexler E, Martin VT, Hutchinson S, Aurora SK, Recober A, Herial NA, Utley C, White L, Khuder SA: Childhood maltreatment and migraine (part II). Emotional abuse as a risk factor for headache chronification. Headache 50:32-41, 2010
- 42. Tietjen GE, Brandes JL, Peterlin BL, Eloff A, Dafer RM, Stein MR, Drexler E, Martin VT, Hutchinson S, Aurora SK, Recober A, Herial NA, Utley C, White L, Khuder SA: Childhood maltreatment and migraine (part III). Association with comorbid pain conditions. Headache 50:42-51, 2010
- 43. Walker LS, Beck JE, Garber J, Lambert W: Children's Somatization Inventory: Psychometric properties of the revised form (CSI-24). J Pediatr Psychol 34:430-440, 2009
- **44.** Walker LS, Greene JW: The Functional Disability Inventory: Measuring a neglected dimension of child health status. J Pediatr Psychol 16:39-58, 1991
- **45.** Wolfe F, Clauw DJ, Fitzcharles M-A, Goldenberg DL, Häuser W, Katz RL, Mease PJ, Russell AS, Russell IJ, Walitt B: 2016 Revisions to the 2010/2011 fibromyalgia diagnostic criteria. Semin Arthritis Rheum 46:319-329, 2016
- **46.** Yehuda R, Halligan SL, Grossman R: Childhood trauma and risk for PTSD: Relationship to intergenerational effects of trauma, parental PTSD, and cortisol excretion. Dev Psychopathol 13:733-753, 2001
- **47.** Ziadni M, You DS, Wilson AC, Darnall BD: CARE Scale-7: Development and preliminary validation of a measure to assess factors impacting self-care in chronic pain. Clin J Pain 34:818-824, 2018