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Adverse childhood experiences and multisite pain among adolescents in the United States

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Abstract

Introduction: Childhood adversity can have a lasting negative impact throughout one's life. Youth with pain conditions consistently report a higher rate of adverse childhood experiences (ACEs) when compared with their healthy peers. Adolescents experiencing pain in more than 1 region tend to have greater symptom burden and reduced quality of life. Research on the association between ACEs and multisite pain in adolescents is sparse.

Objectives: The objective of our study was to investigate the association between cumulative ACEs and self-report of multisite pain in early adolescence using data from the Adolescent Brain Cognitive Development study.

Methods: We used a 19-region body map to evaluate the presence of regional pain (1-2 regions) and multisite pain (≥3 regions). We analyzed data using multinominal logistic regression, adjusting for sociodemographic factors including pubertal status, sex, race/ethnicity, and income-to-needs ratio.

Results: We included a total of 7582 children aged 12 to 13 years, with 33.4%, 24.0%, 13.2%, and 8.6% reporting 1, 2, 3, and 4+ ACEs, respectively. Moreover, 30.7%, 24.2%, 15.2%, and 10.1% of children with multisite pain reported 1, 2, 3, and 4+ ACEs, respectively. Those with 4+ ACEs (adjusted odds ratio 1.62, 95% confidence interval 1.24-2.12) and 3 ACEs (adjusted odds ratio 1.44, 95% confidence interval 1.14-1.82) were more likely to report multisite pain compared with the children with no ACEs.

Conclusion: We showed a potential dose–response relationship between cumulative ACEs and multisite pain, suggesting that the impact of ACEs on pain, particularly multisite pain, may emerge earlier than previously documented.

Keywords:
Adverse childhood experiences, Multisite pain, Adolescent pain

1. Introduction

Multisite pain, which refers to pain distributed across more than 1 body region is relatively common, affecting 1 in 3 youth in community samples and as many as 3 of 4 adolescents with chronic pain.[9,25,26,46] Young individuals experiencing multisite pain tend to report higher pain intensity, greater disability, increased psychological symptoms, and a diminished quality of life when compared with those with pain limited to a single site.[22,27,39,54] Adverse childhood experiences (ACEs) are potentially traumatic events in childhood (between 0 and 18 years of age) that includes maltreatment and abuse as well as living in an environment harmful to development including physical abuse, sexual abuse, household dysfunction, neglect, and parents' divorce/separation.[5,13] Adverse childhood experiences have been identified as a risk factor for chronic pain and adverse health outcomes, with multiple retrospective population-based studies demonstrating a significant number of adults with chronic pain and high impact pain reporting a history of ACEs.[5,6,15,20,33,34] Possible mechanisms connecting childhood adversity to future pain development include the dysregulation of

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centrally mediated stress–response mechanisms, significant biological alterations, and modifications in the maturation and responsiveness of the nervous, endocrine, and immune systems.[1,2,12] Although the prospective association between a history of ACEs and negative life course outcomes including poor health, social, mental, behavioral, and developmental delays have been reported in adults,[11,20] little is known about if these adverse experiences contribute to new onset pain, and more specifically multisite pain in early adolescence. In addition, most of the previous studies examining relationships between ACEs and pain used either retrospective recall of childhood experiences in adult participants or analysis of solely parent-reported data, which raises concerns regarding the validity and reliability of these reports.[15,20,33] This knowledge gap bears significance because of mounting evidence, suggesting that timely interventions focused on families, such as parent education, mental health counseling, and home health visits, may reduce the impact of ACEs on childhood health outcomes and youth/young adulthood may represent a critical time for intervention to prevent greater pain-related issues.[28,32]

The Adolescent Brain Cognitive Development (ABCD) study is the largest long-term prospective study on brain development and adolescent health in the United States with almost 12,000 participants enrolled at baseline across 21 research sites.[14] Within the ABCD study, participants answer questions on a multitude of factors across clinical, biological, and social domains. Importantly, ABCD data collection began early in adolescence, therefore lending us insights into early manifestations of pain, as opposed to many studies where the individuals have had chronic pain for a long time and ask to recall experiences from their childhood.

The primary objective of this study was to evaluate the association between cumulative ACEs and the presence of multisite pain in adolescents. We hypothesized that greater ACE exposure would be associated with a higher odds of reporting multisite pain, even after adjusting for sociodemographic factors.

2. Methods

We analyzed prospective data from the ABCD study to address our study aims. Children were aged between 9 and 10 years when the ABCD study started (year 0, baseline assessment; 2016-2018). In the current study, we used year 2 as our index (second-year follow-up assessment, data release 4.0; children aged between 12 and 13 years), as our dependent variable was introduced in this assessment. We obtained data for covariates and history of ACEs from baseline, first-year follow-up, and second-year follow-up assessments. The study was approved by the Institutional Review Board at the University of Michigan.

2.1. Exclusion criteria

Adolescent Brain Cognitive Development Release 4.0 included 10,414 participants in the second follow-up year. We excluded those with missing demographic information (sex assigned at birth, race/ethnicity, pubertal status, and household income) and those missing responses on any ACE domain. Participants who reported having cancer, cerebral palsy, epilepsy, lead poisoning, muscular dystrophy, multiple sclerosis, and sickle cell anemia at the 2-year follow-up visit or earlier were also excluded from study because of the potential confounding effects caused by pre-existing medical conditions. Recognizing the similarity of a single familial environment, we also excluded siblings' data to remove unwanted dependencies. Hence, only 1 child's data from each family was included. The final sample of the present study comprised 7582 participants (**Fig. 1**).

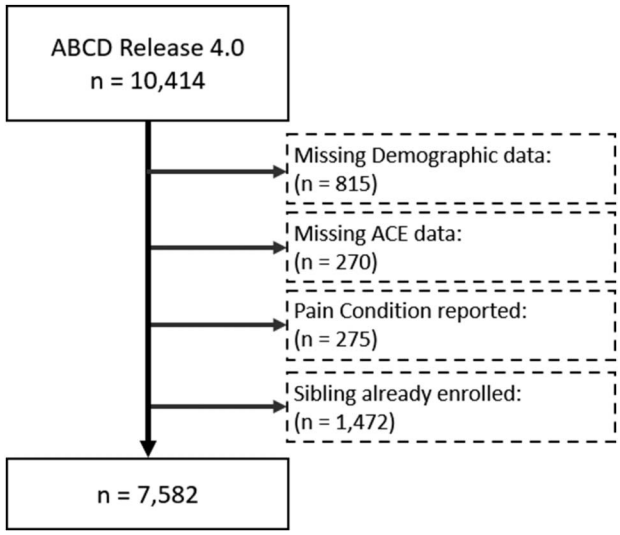

Figure 1. Consort diagram for sample exclusion. Missing demographic information includes sex, race/ethnicity, pubertal status, and income-to-needs ratio. Participants with past or current cancer/leukemia, cerebral palsy, epilepsy, lead poisoning, muscular dystrophy, multiple sclerosis, or sickle cell anemia were excluded. To reduce unwanted dependencies, no instances of 2 or more children residing in the same household were included. ABCD, Adolescent Brain and Cognitive Development; ACE, adverse childhood experience.

2.2. Pain measures

Adolescents who self-reported having had any aches or pains in their body over the past month were asked to identify the locations of their pain on a modified version of the Collaborative Health Outcomes Information Registry (CHOIR) body map.[42] In the ABCD Study, the CHOIR body map depicts both anterior and posterior body sites (38 and 36 sites total, respectively) and includes an additional mouth region, which was not included in the original CHOIR body map.[42] We chose to map the CHOIR body map regions onto the 19 regions in body map by Wolfe et al. to more closely align with the method by which pain widespreadedness is assessed.[53] In this study, we intentionally excluded the mouth region because it is not on the body map by Wolfe et al. (see Supplemental Fig. S1, available at http://links.lww.com/PR9/A309). The body map by Wolfe et al. has been shown to have clinical utility for adults and has been used in studies with children and adolescents.[50]

Definitions of multisite pain vary widely across different populations with little to no consensus.[51] The current study's definitions of multisite and regional pain were based on those found in the literature on multisite pain in children[17,46] while also considering its clinical utility. We grouped participants into 3 categories based on child report of no pain (0 body regions endorsed), regional pain (1-2 regions), and multisite pain (≥3 regions).

2.3. Adverse childhood experiences measure

Consistent with prior research examining ACEs in the ABCD cohort, we identified the presence/absence of 9 domain-specific ACEs from items across 8 validated measures, using both parent and youth reports (see Supplemental Table S2,

available at http://links.lww.com/PR9/A309).[31] The ABCD study reflects 9 of 10 domains listed in the original ACEs Study[13]: physical abuse, sexual abuse, household violence, household alcohol abuse, household mental illness, parents' divorce/separation, household involvement with the criminal justice system, emotional neglect, and physical neglect.[13,31] With the exception of parents' divorce or separation and emotional neglect, each domain included more than 1 item. The structure of the ABCD Study is such that some surveys were given once at baseline, whereas others were given at varying intervals. To ensure adequate coverage of ACE history, we took a liberal approach to classifying a response as positive for the presence of an ACE. First, we determined for each survey item (at any given time point), whether there was evidence of the domain-specific ACE associated with that item. For each item, if a response remained absent across all time points in which the question was asked, then this specific question was coded as missing for this participant. Second, we examined all survey questions in each ACE domain collectively. If a participant responded "yes" to 1 or more of the questions in any of the 3 years, the response was classified as positive for the ACE domain. The absence of any positive response was interpreted as the absence of evidence for that particular ACE domain.

Next, the 9 ACE categories were aggregated into a single, cumulative ACE score. We summed the number of ACE domains endorsed for each participant, with possible scores ranging from 0 to 9, then categorized the continuous score into groups representing 0, 1, 2, 3, and 4 or more ACEs to be consistent with the literature.[15,31,38] The 4+ threshold was considered because it has shown to be a valid threshold indicating increased cumulative risk across multiple ACE screening tools.[15,21,29,38]

2.4. Covariates

2.4.1. Pubertal status

The questions related to body development were asked in the Youth Pubertal Development Scale and Menstrual Cycle Survey History with puberty status range of (1.0-4.0). Consistent with prior research, we used the average score of child self-rated Pubertal Development Scale items that included 5 physical characteristics.[18,23,35] If participants answered at least 4 of the 5 items, a score was calculated. Higher scores are indicative of later stage puberty.

2.4.2. Sex and race

Child's sex assigned at birth and race/ethnicity were collected at baseline. Given the relatively small number of participants who were non-Hispanic Black, Asian, or another race/ethnicity with multisite pain, we categorized race into non-Hispanic White and Other.

2.4.3. Income-to-needs

Socioeconomic status was assessed with an income-to-needs ratio, which quantifies level of household income while accounting for family size, creating a more robust measure of a child's socioeconomic status compared with relying on income alone.[37] This ratio was derived by dividing the median of the reported income range, per parent-report, by the corresponding federal poverty line for the respective family size. A value of 1 in the ratio represents a household at the federal poverty line based on their income and household size. Values lower than 1 represent households below the federal poverty line; values greater than 1 above the poverty line.

2.5. Statistical analysis

Descriptive statistics were computed to describe sample characteristics both overall and by pain group. Mean ± SD and frequencies (n [%]) were used to summarize parametric and nonparametric data, respectively.

To estimate the strength of the associations between number of ACEs (0, 1, 2, 3, and 4+) and presence of multisite or regional pain, we applied multinomial logistic regression techniques, and variables of interest were treated as categorical variables. Specifically, we estimated separate odds of being in the regional pain or multisite pain group (vs no pain) based on membership in 1, 2, 3, and 4 or more ACEs group (vs no ACEs), respectively. Models were adjusted for participant sex, pubertal status, race/ethnicity, income-to-needs ratio, and ACE exposure. We obtained adjusted odds ratio with 95% confidence intervals and selected 0.05 as statistical significance threshold.

All statistical analyses and plots were performed by R Statistical Software (v4.1.1; R Core Team 2022).

3. Results

In total, 7582 children (46.3% female, 54.8% non-Hispanic White) were included in our analysis, with a mean income-to-needs ratio of 3.80 (SD = 2.47) and pubertal status of 2.12 (SD = 0.66) (**Table 1**). Mean pubertal status and income-to-needs ratio were higher in the multisite pain group compared with the regional pain and no pain groups. In addition, non-Hispanic White children composed a higher percentage of the multisite pain group rather than regional and no pain groups. Analysis of missing data showed that participants in the current study were slightly more likely to be assigned female sex at birth, report non-Hispanic White race/ethnicity, and higher income-to-needs ratio (see Supplementary Table S1, available at http://links.lww.com/PR9/A309).

As **Table 1** shows, 63.8%, 22.3%, and 13.8% of the sample reported no pain, regional pain, and multisite pain, respectively. Overall, 20.8%, 33.4%, 24.0%, 13.2%, and 8.6% of total sample reported 0, 1, 2, 3, and 4+ ACEs, respectively.

Among the 9 domains of ACEs, the most commonly reported were household violence (55.5%), household mental illness (31.8%), household involvement with the criminal justice system (29.8%), divorce/separation (17.6%), and household alcohol abuse (14.3%). Of the 270 individuals who were excluded because of missing ACE data at all timepoints, 243 (90.0%) were missing household involvement in the criminal justice system, 228 (84.4%) were missing data on household mental illness, 2 (0.7%) on emotional neglect, and 1 (0.4%) on physical neglect.

Multinomial logistic regression analyses showed that children who reported 4+ vs 0 ACEs had 1.62 times higher odds of experiencing multisite pain than of experiencing no pain. Furthermore, later pubertal status and higher income-to-needs ratios were associated with greater odds of experiencing multisite pain. Participants who reported a race or ethnicity other than non-Hispanic White had significantly lower odds of reporting multisite pain. Similarly, participants who reported 4+ vs 0 ACEs were 1.77 times more likely to experience regional pain (**Table 2**).

In the multisite pain group, the absolute risk increases with the number of ACEs. Compared with individuals with 0 ACEs, 13.2% of whom reported multisite pain, those with 1 ACE have a 13.3%

Table 1

Demographic variables and adverse childhood experiences.

Variable	Total (n = 7582)	Multisite pain (n = 1049)	Regional pain (n = 1695)	No pain (n = 4838)
Pubertal status, mean (SD)	2.12 (0.66)	2.23 (0.66)	2.16 (0.65)	2.08 (0.66)
Sex				
Female	3508 (46.3)	526 (50.1)	764 (45.1)	2218 (45.8)
Male	4074 (53.7)	523 (49.9)	931 (54.9)	2620 (54.2)
Race/ethnicity				
Non-Hispanic White	4157 (54.8)	635 (60.5)	937 (55.3)	2585 (53.4)
Other	3425 (45.2)	414 (39.5)	758 (44.7)	2253 (46.6)
Income-to-needs ratio, mean (SD)	3.80 (2.47)	3.99 (2.50)	3.92 (2.49)	3.71 (2.44)
Physical abuse	76 (1.0)	10 (1.0)	19 (1.1)	47 (1.0)
Sexual abuse	79 (1.0)	11 (1.0)	20 (1.2)	48 (1.0)
Household violence	4206 (55.5)	582 (55.5)	988 (58.3)	2636 (54.5)
Household alcohol abuse	1083 (14.3)	179 (17.1)	264 (15.6)	640 (13.2)
Household mental illness	2410 (31.8)	401 (38.2)	586 (34.6)	1423 (29.4)
Divorce/separation	1338 (17.6)	199 (19.0)	318 (18.8)	821 (17.0)
Household involvement with the criminal justice system	2256 (29.8)	318 (30.3)	537 (31.7)	1401 (29.0)
Emotional neglect	51 (0.7)	6 (0.6)	11 (0.6)	34 (0.7)
Physical neglect	517 (6.8)	70 (6.7)	110 (6.5)	337 (7.0)
ACE score groups				
0	1577 (20.8)	208 (19.8)	324 (19.1)	1045 (21.6)
1	2533 (33.4)	322 (30.7)	565 (33.3)	1646 (34.0)
2	1816 (24.0)	254 (24.2)	383 (22.6)	1179 (24.4)
3	1001 (13.2)	159 (15.2)	238 (14.0)	604 (12.5)
4+	655 (8.6)	106 (10.1)	185 (10.9)	364 (7.5)

Continuous variables are reported as mean (SD) and categorical variables are reported as n (%). Participants were divided into pain groups based on the number of sites they stated they had pain in, 3 or more sites corresponded to multisite pain, 1 to 2 sites was regional pain and 0 sites was no pain. Race/ethnicity groups included in other were non-Hispanic Black, Hispanic, Asian, and other.
ACE, adverse childhood experience.

probability, 2 ACEs have a 15.1% probability, 3 ACEs have an 18.0% probability, and those with 4+ ACEs reported had a 19.8% probability, indicating a 6.6% absolute increase when comparing the 4+ ACE group with the 0 ACE group.

4. Discussion

The present study provides important insights into the relationship between ACEs and multisite pain in early adolescence using a large representative sample of children in the United States. Chronic pain is a serious concern for many children as previous research suggests that ACEs contribute to chronic pain among adolescents and can follow them into adulthood.[15,33] We found that a history of 4+ ACEs was associated with increased likelihood of multisite pain and regional pain. This finding is aligned with previous studies demonstrating associations between cumulative ACEs and increased prevalence of pain sites and pain chronicity in children.[1,6,15,33]

Although it has been reported that nearly 2 thirds of youth experience significant ACEs, the prevalence of ACEs varies considerably across studies ranging from 41% to 97%, which is largely attributed to the definition adopted.[1,7] Thus, the reported rates for 1, 2, 3, and 4+ ACEs in the current study are within the window defined in other studies and also parallels those observed in previous ABCD studies.[21,38] In examining specific ACE domains, we observed that household violence, household mental illness, and household involvement in the criminal justice system were the most reported ACE domains in our sample.

Table 2

Multinomial logistic regression associations between demographics, adverse childhood experiences, and pain.

Variable	Multisite pain		Regional pain	
	OR (95% CI)	P	OR (95% CI)	P
Pubertal status	1.47 (1.31-1.64)	<0.0001	1.29 (1.18-1.42)	<0.0001
Sex (ref. female)				
Male	1.03 (0.88-1.19)	0.7356	1.18 (1.04-1.33)	0.0090
Race/ethnicity (ref. non-Hispanic White)				
Other	0.74 (0.64-0.85)	<0.0001	0.95 (0.84-1.07)	0.4096
Income-to-needs ratio	1.05 (1.02-1.08)	0.0030	1.05 (1.02-1.08)	0.0002
ACE exposure (ref. 0)				
1	1.01 (0.83-1.23)	0.9034	1.13 (0.96-1.32)	0.1387
2	1.17 (0.95-1.44)	0.1344	1.10 (0.92-1.31)	0.2867
3	1.44 (1.14-1.82)	0.0023	1.34 (1.10-1.64)	0.0036
4+	1.62 (1.24-2.12)	<0.0001	1.77 (1.42-2.22)	<0.0001

Multinomial logistic regression model comparing multisite and regional pain to the no pain group.
ACE, adverse childhood experience; CI, confidence interval; OR, odds ratio.

Furthermore, our reported domains differed slightly in prevalence compared with those reported in other studies among US youth and adult population. Relative to other ABCD cohorts, the current study population had a lower rate of household alcohol abuse, likely because of the narrower degree of relationship in our definition of alcohol abuse (ie, parental instead of any blood relative[26]). In addition, ACE domains including physical and sexual abuse were only asked of the parent and not of the child. This lack of child-report data for these specific domains may have led to underreporting of the true prevalence of these ACE domains. However, it should be noted that there is great variability in assessment methods, ACE measures, and population characteristics (such as age and socioeconomic status) in the literature, making it difficult to define and estimate the prevalence of ACEs consistently across studies.

We found that children with a greater number of ACEs were more likely to report multisite pain. Specifically, those with 4+ ACEs had higher odds of experiencing multisite pain compared with those with no reported ACEs. This association underscores the cumulative risk that exposure to multiple ACE domains can have on the development of more complex pain profiles, such as multisite pain. Although we did not have specific hypotheses concerning the relationship with regards to a participant's pubertal status and race and ethnicity, some notable similarities and differences from the literature were noted.

Consistent with prior analyses in the ABCD cohort, we found that later pubertal status was associated with greater report of multisite pain. Furthermore, we also found that children who identify as a racial or ethnic group other than non-Hispanic White exhibited a lower likelihood of self-reporting instances of multisite pain, which is consistent with previous findings in the literature.[45] It is uncertain why multisite pain was less common among non-White groups in the current study and may be because of stigma or biases directed at people of color who have pain symptoms, which can affect self-perceptions and willingness to disclose health-related information.[4,40,52] For example, qualitative date from older Black adults dealing with chronic pain highlights themes of enduring or living with pain cautiously, deciding carefully when and with whom to share such information[4,40] such that pain symptoms may be underreported in these groups relative to White peers within the context of research.

This study has many strengths, including its large, nationally representative sample and the use of both parent and child report for ACE exposures to assist in reducing recall bias and underreporting. Despite these significant strengths, several limitations should be acknowledged. First, the causal relationship between cumulative ACEs and multisite pain cannot definitively be determined because of the timing in which ACEs were collected in proximity to when the pain measure was collected. Despite the rigorous stratified sampling strategy used by the ABCD study, and the resultant diversity of the sample, the potential for selection bias cannot be dismissed, particularly given inclusion constraints. Indeed, the resulting sample has a higher family income and urban residency compared with the general population, partially because of participants being required to live within 50 miles of 1 of the 21 study sites. This characteristic of the sample may affect their overall health status, including pain and related symptoms as well as exposure to ACEs.[10] This potential for selection bias cannot be dismissed and may limit the generalizability of the results. Finally, perhaps attributed to the fact that a significant portion of the young adolescents in our sample had not yet reached the advanced stages of puberty, or had not completed it altogether, we did not observe and statistically significant differences in the prevalence of multisite pain between boys and girls.[36,47] Previous research suggests that prepubertal boys and girls display similar rates of multisite pain; however, as they progress through puberty and into adulthood, females begin to report significantly greater rates of multisite pain.[36,47]

The mechanisms linking ACEs and multisite pain are likely complex and multifaceted. Severe adversity experienced in early life may become biologically embedded, thereby deleteriously affecting functioning across multiple body systems.[3] For example, previous studies suggest that a risky and harsh family environment can lead to an exaggerated pro-inflammatory and biological response to potentially threatening stimuli, which can remain chronically activated leading to allostatic overload.[12,30] A pro-inflammatory milieu has been linked to widespread pain.[43,44] Traumatic stress is also associated with neurobiological changes related to external and internal sensory perception.[16] The brain regions that show structural and functional changes in relation to traumatic exposure (eg, insula) have also been highlighted as key regions relevant to widespread pain.[48] Co-occurring symptoms resulting from trauma exposure, such as disturbed mood and sleep problems, may also play important roles in the genesis and continuation of widespread pain.[8,16,19,24,30,41]

Future research should investigate whether there are vulnerable periods in the development of multisite pain, including those during puberty, early-onset puberty, and childhood stages (early childhood vs late adolescence). It would also be beneficial to determine the relative contribution of specific ACE domains to multisite pain. Identifying the driving ACE domains could then serve as a targeted approach for further screening, and intervention strategies such as providing trauma-informed care pain management.[49] In addition, future research should work to evaluate if individuals with ACE exposure may require different treatment approaches for chronic pain compared with those without this trauma exposure. This includes experiences with specific ACE domains and how they may influence treatment resistance to certain pain therapies or other psychological/behavioral therapies. This proactive approach may facilitate early identification and intervention for children at risk of ACE-related pain.

5. Conclusion

This study established an association between the accumulation of ACEs and the manifestation of regional and multisite pain in early adolescence. These findings suggest that the relationship between ACEs and pain emerges at an earlier stage of development than previously documented.

Disclosures

The authors have no conflicts of interest to declare.

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Supplemental digital content

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