Published in final edited form as:

J Clin Psychol. 2017 October ; 73(10): 1403–1428. doi:10.1002/jclp.22444.

When Emotional Pain Becomes Physical: Adverse Childhood Experiences, Pain, and the Role of Mood and Anxiety Disorders

Natalie J. Sachs-Ericsson[1], **Julia L. Sheffler**[1], **Ian H. Stanley**[1], **Jennifer R. Piazza**[2], and **Kristopher J. Preacher**[3]

[1]Florida State University

[2]California State University, Fullerton

[3]Vanderbilt University

Abstract

Objective: We examined the association between retrospective reports of adverse childhood experiences (ACEs) and painful medical conditions. We also examined the mediating and moderating roles of mood and anxiety disorders in the ACEs–painful medical conditions relationship.

Method: Ten-year longitudinal data were obtained from the National Comorbidity Surveys (NCS-1, NCS-2; $N = 5001$). The NCS-1 obtained reports of ACEs, current health conditions, current pain severity, and mood and anxiety disorders. The NCS-2 assessed for painful medical conditions (e.g., arthritis/rheumatism, chronic back/neck problems, severe headaches, other chronic pain).

Results: Specific ACEs (e.g., verbal and sexual abuse, parental psychopathology, and early parental loss) were associated with the painful medical conditions. Baseline measures of depression, bipolar disorder, and posttraumatic stress disorder were also associated with the number of painful medical conditions. Anxiety and mood disorders were found to partially mediate the ACEs–painful medical conditions relationship. We determined through mediation analyses that ACEs were linked to an increase in anxiety and mood disorders, which, in turn, were associated with an increase in the number of painful medical conditions. We determined through moderation analyses that ACEs had an effect on increasing the painful medical conditions at both high and low levels of anxiety and mood disorders; though, surprisingly, the effect was greater among participants at lower levels of mood and anxiety disorders.

Conclusion: There are pernicious effects of ACEs across mental and physical domains. Dysregulation of the hypothalamic-pituitary-adrenal stress response and the theory of reserve capacity are reviewed to integrate our findings of the complex relationships.

Keywords

adverse childhood experiences; anxiety and mood disorders; painful medical conditions

Please address correspondence to: Natalie Sachs-Ericsson, PhD, Department of Psychology, Florida State University, Tallahassee, FL, 32306-1270. sachs@psy.fsu.edu.

Early life stressors have profound effects on subsequent health and psychological functioning. The stress associated with adverse childhood experiences (ACEs)—such as parental physical, sexual, and verbal abuse; parental psychopathology; early parental loss; and low family of origin income—has been found to affect basic biological and neural processes during development (Heim & Nemeroff, 2002; Nemeroff, 2016). The experience of chronic stressors associated with ACEs appears to alter physiological and behavioral responses to subsequent stress, possibly through dysregulation of the hypothalamic-pituitary-adrenal (HPA) axis and the autoimmune system, which may underlie increased risk for mood and anxiety disorders as well as pain-related medical conditions. Whereas these physiological changes and behavioral adaptations may start early in life, the consequences for psychological and physical health may exert themselves many decades later. Moreover, those who are exposed to adversity early in life may not develop adequate coping mechanisms (see reserve capacity model in Gallo, 2009), which increases their vulnerability to subsequent stressors throughout the lifespan, affecting health outcomes as one ages.

Definition of Childhood Abuse and ACEs

Whereas the long-term consequences of childhood physical and sexual abuse have received considerable scientific investigation, recent studies have sought to extend these findings by focusing on the consequences of a range of ACEs. Definitions of childhood abuse and neglect include both qualitative and quantitative aspects (Glaser, 2000): They comprise single events, repeated events, or patterns of interactions between the child and the caretaker. Perhaps the most well-known conceptualization of ACEs has been derived from the ongoing Adverse Childhood Experiences (ACEs) Study (Dube et al., 2003; Felitti, 1998). Their measures of ACEs are childhood emotional, physical, sexual abuse, parental psychopathology, substance abuse, and early parental loss (due to death/abandonment, or parental incarceration). Importantly, both the number and the severity of ACEs are associated with poor health outcomes across multiple physical and mental health domains (Anda et al., 2006; Björkenstam; Widom, Czaja, Bentley, & Johnson, 2012).

Given the different indices and definitions of childhood abuse across studies, in the current review, we apply the term *ACEs* when a study used a comprehensive definition of abuse as described in the ACEs Study (Dube et al., 2003; Felitti, 1998). In contrast, if the study was limited to a specific form of abuse (e.g., physical or sexual abuse), we simply have specified the specific type of abuse.

Retrospective reports of ACEs.

The vast majority of publications examining the effects of ACEs have used retrospective reports of abuse obtained from the participant in adulthood. The retrospective nature of this type of assessment has led to much discussion regarding the validity and reliability of retrospective reports. A series of studies evaluating the validity and reliability of such reports have generally supported this methodology (Pinto, Correia, & Maia, 2014; Widom & Shepard, 1996), although one area of concern has been the underreporting of abuse experiences (e.g., false negatives; Dube, Williamson, Thompson, Felitti, & Anda, 2004).

For example, in a large review of the literature on retrospective reports of abuse, researchers (Hardt & Rutter, 2004) identified studies (between 1980 and 2001) in which there were well-quantified assessments of the validity of retrospective recall of sexual abuse, physical abuse, physical/emotional neglect, or family discord. Validity was assessed with comparisons to contemporaneous, prospectively obtained court, clinic, or research records, or by agreement between retrospective reports of two siblings. The researchers found the retrospective reports in adulthood of ACEs involved a substantial rate of false negatives (e.g., underreporting). However, false positives are rare. Researchers concluded that potential bias in retrospective reports of ACEs is not sufficient to invalidate retrospective case control studies of ACEs. However, the effects of underreporting should be taken into consideration.

ACEs and Painful Medical Conditions

There is an established association between retrospective reports of childhood abuse experiences and adult pain-related medical conditions (Brown, Berenson, & Cohen, 2005; Davis, Luecken, & Zautra, 2005; Green, Flowe-Valencia, Rosenblum, & Tait, 2001; Irish, Kobayashi, & Delahanty, 2009; Sachs-Ericsson, Kendall-Tackett, & Hernandez, 2007). A relatively high proportion of patients with chronic pain-related medical conditions have a history of childhood physical or sexual abuse (Bailey, Freedenfeld, Kiser, & Gatchel, 2003; Davis et al., 2005). In epidemiological studies, researchers have found an association between childhood exposure to maltreatment (e.g., sexual or physical abuse) and subsequent pain-related disorders in adulthood (Brown et al., 2005; Leserman, 2005; Romans, Belaise, Martin, Morris, & Raffi, 2002; Sachs-Ericsson et al., 2007; Thompson, Kingree, & Desai, 2004; Walsh, Jamieson, MacMillan, & Boyle, 2007a,b).

In a meta-analytic review, researchers concluded that individuals from the community reporting pain-related medical conditions were more likely to have been abused or neglected than individuals not reporting pain-related conditions (Davis et al., 2005). In a cross-sectional epidemiological study using data from 10 countries (Scott et al., 2011), researchers found that three or more ACEs were associated with an increased prevalence of all medical disorders, including pain-related conditions. However, not all studies have found an association between childhood abuse and adult reports of pain (Raphael, Chandler, & Ciccone, 2004).

Whereas the scientific study of the association between ACEs and negative health consequences, such as painful medical conditions, has expanded dramatically over the past few decades, so has the study of *pain-related medical conditions of aging*. The prevalence of several pain-related medical conditions such as arthritis, neck pain, or back pain has been found to increase with age (Chalan, van den Berg, Kroesen, Brouwer, & Boots, 2015; Smith, Davis, Stano, & Whedon, 2013). There are some unique characteristics of painful medical conditions associated with the aging process. As individuals age, researchers have found that there is an increased vulnerability to neuropathic pain (Gagliese, 2009). Moreover, older adults reporting painful medical conditions are more likely to endorse multiple sites of pain compared to younger adults (Patel, Guralnik, Dansie, & Turk, 2013).

From evidence across numerous studies, researchers have concluded that the effects of ACEs on physical and mental health conditions persist throughout the life course (Draper et al., 2008; Sachs-Ericsson et al., 2010; Sachs-Ericsson, Medley, Kendall–Tackett, & Taylor, 2011; Sachs-Ericsson, Rushing, Stanley, & Sheffler, 2016). For example, in a large population-based cohort study of middle-aged men and women, researchers found that retrospective reports of childhood physical abuse were associated with worse physical health decades after the abuse (Springer, Sheridan, Kuo, & Carnes, 2007).

Additionally, researchers have found that physical, sexual, and emotional abuse and neglect are related to inflammation in middle-aged women, increasing the risk for multiple chronic diseases that have an inflammatory pathophysiology (e.g., cardio-vascular diseases and diabetes; Matthews, Chang, Thurston, & Bromberger, 2014). Davis and colleagues (2005), reviewed evidence that people exposed to major stressors in early life have elevated rates of morbidity and mortality from chronic diseases of aging. Compelling data come from studies of children who were raised in poverty or maltreated by their parents that show heightened vulnerability to vascular disease, autoimmune disorders, and premature mortality (Davis et al., 2005; Sachs-Ericsson et al., 2011). Thus, in general, painful medical conditions tend to increase with aging, and the effects of ACEs may continue to exert influence throughout the aging process.

ACEs, Mood, and Anxiety Disorders

In epidemiological studies, researchers have shown that ACEs increase the risk for most psychiatric disorders (Edwards, Holden, Felitti, & Anda, 2003; Green et al., 2010; Polusny & Follette, 1995), and this risk does not attenuate with age (Clark, Caldwell, Power, & Stansfeld, 2010). In one study, researchers concluded that the estimated attributable fractions for psychiatric disorders related to having experienced any single ACE (e.g., childhood physical or sexual abuse, domestic violence) ranged from 22% to 32% among women and 20% to 24% among men (Afifi et al., 2008).

Researchers have identified a particularly strong link between childhood abuse, neglect, and mood and anxiety disorders (Cougle, Timpano, Sachs-Ericsson, Keough, & Riccardi, 2010; Heim, Newport, Mletzko, Miller, & Nemeroff, 2008; Heim, Shugart, Craighead, & Nemeroff, 2010; Liu, Jager-Hyman, Wagner, Alloy, & Gibb, 2012; Maniglio, 2013; Sachs-Ericsson et al., 2010; Sachs-Ericsson, Verona, Joiner, & Preacher, 2006). For example, researchers, conducting a meta-analysis, demonstrated that those with a history of childhood abuse (sexual and physical) had a significantly greater risk for depression and anxiety (Lindert et al., 2014). In a recent review of the literature (including four meta-analyses, N = 3,214,482 from 171 studies), researchers found evidence that retrospective report of childhood sexual abuse was a significant risk factor for anxiety disorders (Maniglio, 2013).

ACEs, Mood and Anxiety Disorders, and Chronic Pain Conditions

Researchers using population-based studies have also found associations among ACEs, mood and anxiety disorders, and pain-related medical conditions (Raphael & Widom, 2011; Scott et al., 2011; Walsh et al., 2007b). For example, in a longitudinal population study

(Gonzalez et al., 2012), researchers found that a comprehensive retrospective measure of ACEs was related to comorbid depression and chronic pain conditions. Similarly, in a large cross-sectional international study (Scott et al., 2011), researchers found that retrospective reports of ACEs were associated with early-onset anxiety and mood disorders and subsequent pain-related medical conditions.

Mediating/Moderating Role of Mood and Anxiety Disorders in the ACEs–Pain Association

The associations among ACEs, health, and pain-related problems may, in part, be due to the higher rates of psychiatric problems found among those with ACEs. Several studies have examined the role of psychiatric disorders as both a *mediator* and a *moderator* of the association between ACEs and pain. A moderator is a variable that affects the *direction and/or strength* of the relation between the predictor variable and the criterion variable. That is, anxiety and mood disorders may exacerbate the effects of ACEs on pain conditions. This has commonly been referred to as an *interaction* of two variables (Preacher, Curran, & Bauer, 2006). In mediation analyses, conceptually, the predictor variable (such as ACEs) is thought to cause the mediator (such as anxiety and mood disorders), and, in turn, the mediator increases the risk of the criterion variable (such as pain-related medical conditions): “Whereas moderator variables specify when certain effects will hold, mediators speak to how or why such effects occur” (p. 1176, (Baron & Kenny, 1986). A variable may serve as both a mediator and a moderator.

As we will examine in the current study, first, it may be the case that ACEs and mood/anxiety disorders independently contribute to pain-related medical conditions (main effects model). Second, it may also be the case that the presence of mood and anxiety disorders may exacerbate the negative effects of ACEs on painful medical conditions (i.e., moderation). Finally, ACEs may directly affect the onset of anxiety/mood disorders, which, in turn, leads to painful medical conditions (i.e., mediation).

In this regard, findings of extant studies have been equivocal in part because of inconsistent definitions of ACEs and pain-related conditions as well as the use of different measures of psychopathology. For example, in one population study of women, anxiety, depression, and substance abuse failed to mediate the relationship between physical abuse and chronic pain reports (Walsh et al., 2007b). In another cross-sectional population study, based on the first wave of the National Comorbidity Survey (NCS-1) data, adult survivors of childhood sexual and physical abuse were found to have more health problems including painful medical symptoms; psychiatric disorders were found to account for some, but not all, of these symptoms (Sachs-Ericsson, Blazer, Plant, & Arnow, 2005). However, in another large cross-sectional international study (Scott et al., 2011), researchers found that retrospective reports of ACEs independently predicted both early onset mental health problems and several pain-related medical disorders; yet mental health problems did not mediate or moderate the association between ACEs and the painful medical conditions.

In one of the only prospective studies, researchers used a cohort sampling stratification method in which court-documented abused and/or neglected children were matched with

nonabused children and followed into adulthood (Raphael & Widom, 2011). Whereas researchers found that documented abuse predicted subsequent adult pain complaints, posttraumatic stress disorder (PTSD) did not mediate the relationship between childhood victimization and pain reports. Nonetheless, PTSD robustly interacted with documented childhood victimization (i.e., moderation) to predict adult pain. That is, individuals with both childhood abuse and PTSD were at a significantly increased risk of pain-related conditions. In light of these discrepant findings, it is important to conduct further scientific inquiry in this area.

The Present Study

In previous cross-sectional analyses based on the baseline NCS-1 data (Sachs-Ericsson et al., 2005), participants who retrospectively reported childhood physical and/or sexual abuse were found to have more health problems and higher levels of pain reports in relation to their health problems compared to participants without abuse histories (Sachs-Ericsson et al., 2007). In the current longitudinal study, analyses of the baseline NCS-1 data are extended to determine if retrospective reports of ACEs obtained at baseline (i.e., NCS-1) are associated with the pain-related medical conditions at follow-up (i.e., NCS-2).

To that end, the current study used data from the baseline NCS-1 and 10-year follow-up (NCS-2) to investigate the association between retrospective reports of ACEs, assessed at baseline, and the number of painful medical conditions occurring over the follow-up period (e.g., NCS-2). Retrospective reports of ACEs were obtained using a comprehensive measure of several adverse childhood experiences that took into consideration the frequency and severity of the ACEs. Further, at baseline we examined the role of mood (i.e., major depression, bipolar) and anxiety (i.e., generalized anxiety disorder [GAD], panic disorder, PTSD, social phobia) disorders in the association between ACEs and pain conditions. We posited three hypotheses that are not mutually exclusive.

- Main effects model: ACEs and mood and anxiety disorders independently and directly contribute to pain-related medical conditions.
- Moderation model: The combined presence of baseline mood and anxiety disorders potentiates the negative effects of ACEs on the development of pain-related medical conditions.
- Mediation model: ACEs increase the risk of mood and anxiety disorders, and, in turn, mood and anxiety disorders contribute to the development of pain-related conditions.

Method

Participants and Procedures

The sample includes 5,001 participants from the NCS-1 and NCS-2 10-year longitudinal-based epidemiological study.

Baseline (NCS-1).—NCS-1 included over 8,000 male and female respondents aged 15 to 55 years (RC Kessler, 1994). The NCS-1 survey was conducted in the early 1990s in the

United States. Part II of the baseline NCS-1, which included questions related to psychosocial correlates of psychiatric disorders, (e.g., retrospective reports of childhood abuse and recent medical problems), was administered to a subsample of respondents (*N* = 5,877) who screened positive for any lifetime diagnosis in Part I, and a random subsample of participants assessed in Part I who did not screen positive for a diagnosis. More detailed descriptions of the NCS-1 sampling design and procedures are reported elsewhere (Kessler, 1994; Kessler et al., 1994; Kessler & Walters, 2003) and are described briefly below.

10-year follow-up (NCS-2).—NCS-2 is a 10-year follow-up of the baseline study (Kessler, 2013). The NCS-2 (N = 5001) included 62% of the original NCS-1 respondents who were administered the entire psychosocial survey at baseline. Of the respondents who were successfully traced, 166 were deceased. Thus, there was a conditional response rate of 87.6% at follow-up (Kessler & Walters, 2003). NCS-2 respondents were assessed using an expanded version of the baseline psychosocial interview. Relevant to the current study, several health problems, which included specific pain-related medical conditions occurring between the waves (e.g., over the 10-year period), were assessed at follow-up. Whereas both the NCS-1 and NCS-2 assessed for arthritis and rheumatoid arthritis, as described below, the NCS-2 included some additional pain-related medical conditions not assessed in the NCS-1 (e.g., back or neck pain, severe and frequent headaches, and any other pain-related conditions).

Relative to the baseline respondents, NCS-2 respondents were significantly more likely to be female, well educated, and residents of rural areas of the United States. A propensity score adjustment weight was derived to correct for these discrepancies (see Rosenbaum & Rubin, 1983). This weighting score was applied to all of the analyses reported in the current manuscript.

Interviewers and Procedures

As reported by Kessler (1994), the NCS was conducted by the field staff of the Survey Research Center at the University of Michigan. The 158 interviewers had an average of 5 years of prior interviewing experience with the Survey Research Center. In addition, the NCS interviewers went through a 7-day training program. Fieldwork was closely monitored throughout the entire data collection period.

Participants were interviewed in their homes, and informed consent was obtained. Several procedures were conducted to improve the reliability of the data, particularly in regard to abuse and traumatic experiences (see Kessler et al., 1998; Kessler & Wethington, 1991). To improve accuracy of participants' responses to the NCS surveys, each interview began with a life review section that provided participants with instructions designed to improve recall and motivate them to answer items honestly (see Kessler, Wittchen, Abelson, & Zhao, 2000).

NCS-1 Baseline Measures.

Demographics.—Participants completed a demographic questionnaire to assess age, sex, race, and education.

NCS-1 Diagnostic and Statistical Manual of Mental Disorders (DSM III-R) (APA, 1987) mood and anxiety disorders.—In this study, the NCS-1 lifetime (e.g., past and/or current history) mood disorders included major depression and bipolar disorder; lifetime anxiety disorders included PTSD, panic disorder, GAD, and social phobia.

Lifetime history of disorder as assessed at baseline.—Lifetime history of each DSM disorder (e.g., past or current) was assessed at baseline. We identified lifetime disorders (e.g., current disorders and/or past history of disorder) because it is important to our theoretical model. The theory underlying our hypotheses is that ACEs negatively affect neurological and physiological mechanisms (via the HPA and immune response) early in life, which then may contribute to the development of psychiatric disorders as well as pain-elated medical conditions (main effects model). It may be the case that the dysregulation of the individual's biological and neurological functioning caused by the ACEs contribute first to the development of the psychiatric disorders, which may, in turn, contribute to the development of pain-related disorders (mediation). Or it may be the case that for individuals with ACEs, the additional presence of psychiatric disorders may exacerbate (moderation model) the pain-related medical conditions. Thus, it is important to obtain past and present history of mood or anxiety disorders to examine these hypotheses

DSM IIIR (APA, 1987) diagnoses.—At baseline, participants' lifetime psychiatric diagnoses (i.e., a diagnosis for which a participant met criteria at some point in their life–past or present) were assessed using the semistructured Composite International Diagnostic Interview (CIDI; World Health Organization, 1990). The CIDI is a standardized diagnostic interview based on the diagnostic criteria of the International Classification of Diseases 10^{th} revision, designed for use in epidemiological studies. Trained interviewers administered a series of questions about psychiatric symptoms, and systematized follow-up probes were included in the CIDI to evaluate symptom severity. The reliability and validity of the CIDI has been established in prior work (Kessler, Sonnega, Bromet, Hughes, & Nelson, 1995).

Briefly, researchers have reported that the CIDI demonstrated good inter-rater reliability within the United States and across countries around the world. In a review of the CIDI, Wittchen (Wittchen, 1994) indicated that studies have shown good test-retest reliability (kappa consistently above 0.6) and good-to-excellent inter-rater reliability (with kappa coefficients ranging from 0.5 to 0.7) across most diagnostic sections. Researchers (Janca, 1992; Wittchen, 1994) have found, that the CIDI has acceptable to good validity indices for most DSM diagnoses (e.g., depressive disorders K = 0.84, anxiety disorders K = 0.76, panic disorder K = 0.84, and substance use disorders K = 0.83).

In should be noted that in epidemiological and other large scale research studies examining the association between child abuse and psychiatric disorders, the standard for assessing psychiatric diagnoses is the CIDI, originally developed by the WHO (1990; see Sareen et al., 2013; Afifi et al., 2008). As Kessler and colleagues (2013) have recently noted, inconsistency in measurement of common mental disorders in primary care and community epidemiological samples impedes progress in clinical epidemiology; thus, they strongly recommend the use of validated assessments based on the CIDI scales in the assessment of anxiety or mood disorders.

The count of anxiety and mood disorders.—The specific baseline psychiatric disorders (e.g., depression, bipolar, PTSD, panic disorder, GAD, social phobia) were included in the Poisson regression analyses to examine the main effects of each disorder in their association with the number of painful medical conditions assessed at follow-up. However, to conduct mediation and moderation analyses, we constructed a count variable of the participant's summed number of lifetime mood and anxiety-related disorders. Thus, the score ranged from 0 to 6.

ACE Measures

Preliminary studies were conducted to determine methods to improve participants' memory and accuracy in their report of childhood abuse. Researchers attempted to improve recall by listing each traumatic event separately and then asking specific questions about each trauma. This methodology has been shown to increase validity and reliability of recall (Kessler & Wethington, 1991). The second modification was to provide the participant with a booklet that listed each trauma separately and refered to each event by number rather than the specific name of the trauma. Previous studies found participants were uncomfortable talking about having been abused in childhood. Referring to the event by number, rather than by the description of the event, was shown to increase reliability (see (Kessler et al., 1999).

Each specific ACE was obtained at baseline. Thus, these are retrospective reports of ACEs. The specific ACEs included in the first regression analyses are described below. The participant rated each of the nine ACEs (with the exception of parental loss) for frequency and severity; thus, with the exception of parental loss, each ACE was a continuous measure representing the frequency and severity of the experience.

Abuse Items: Sexual, Physical, and Verbal

The interviewer provided the participant with a booklet listing each of the traumatic events. The participant was asked to look at the list of traumatic event and indicate to the interviewer the number representing each of the events experienced in their lifetime.

Sexual abuse by parent or relative.—The sexual abuse items were embedded in the PTSD module of the CIDI, which has been shown to have good validity and reliability (Kessler, 2000). For the present study, respondents who reported that they had *not* been raped or molested by a parent (or step-parent/relative) before the age of 15 were coded 0. Respondents who reported having been raped or molested by a parent (or step-parent/relative) before the age of 15 *on only one occasion* was coded 1. Respondents who reported having been raped or molested by a parent (or stepparent/relative) before the age of 15 and the abuse had occurred *more than once* were coded 2.

Parental verbal abuse.—The parental verbal abuse item was embedded in the childhood history section of the NCS-1. Participants reviewed a list of specific behaviors related to verbal abuse (insulted, swore at, did or said something to spite, threatened to hit) and indicated how often a parent or stepparent did any of these things on the list to them during childhood. Participants were coded for parental verbal abuse as follows: 4 = often, 3 = sometimes, 2 = rarely, or 1 never).

Parental physical abuse.—The parental physical abuse item was embedded in the childhood history section of the NCS-1. Participants were asked if they had experienced physical abuse by their parent or stepparent (e.g., pushed, grabbed, or shoved, kicked, bit, hit with a fist, hit with something, beat up, choked, or burned). Participants were coded for parental abuse as follows: 4 = often, 3 = sometimes, 2 = rarely, or 1 = never).

Early parental loss due to divorce, abandonment, or death before the age of 15.—Participants were asked several questions regarding their family life to determine whether the participant had experienced early parental loss (due to death of a parent, prolonged separation due to divorce, or abandonment) before the age of 15 (yes = 1/no = 0).

Family-of-origin economic functioning.—Participants were asked to compare their family of origin's financial status during most of their childhood to the average family in their community and rate it on a scale from 1 (*better off*) to 5 (*a lot worse off*).

Mother and father's externalizing and internalizing psychiatric symptoms count.—We assessed parental psychiatric symptoms using the Family History Research Diagnostic Criteria (FHRDC; Andreasen, Endicott, Spitzer, & Winokur, 1977). In general, past researchers have found the diagnostic inter-rater reliability was good to excellent for specific FHRDC disorders K ranged from .66 to .73 (Zimmerman, Coryell, Pfohl, & Stangl, 1988).

Four separate continuous variables were computed to derive a symptom count of mother's and father's internalizing and externalizing symptoms. Using the Family History Research Diagnostic Criteria (Andreasen et al., 1977), participants were asked about their parents' symptoms of depression and anxiety (i.e., internalizing symptom count), use of drug and alcohol, and symptoms of antisocial personality disorder (i.e., externalizing symptom count). We then derived a symptom count score, representing the number of symptoms endorsed for each parent for internalizing and externalizing disorders.

Simple ACEs count.—We derived a simple ACE count. For this count variable, we coded each of the ACEs dichotomously (e.g., any verbal abuse: yes = 1/no = 0). The simple ACEs count could vary from 0 to 9, and was used in creating the mediation and moderation models. The ACE count was also used for descriptive purposes in the tables and figure.

Additional Covariates

Baseline health.

Health problems at baseline.: We included the participant's number of health problems, as assessed at baseline, as a covariate. To increase validity and reliability of the baseline health reports, participants were asked to review a list of serious health problems and indicate if they had experienced any of these problems during the 12 months prior to the interview. The health problems were as follows: AIDS, arthritis or rheumatism, asthma, being blind or deaf, bronchitis or tuberculosis, cancer, diabetes, high blood pressure or hypertension, heart problems, hernia, kidney or liver disease, lupus, thyroid or autoimmune disorders, neurological problems, stroke, stomach or gallbladder disease, or ulcers.

The NCS survey attempted to improve the accuracy of recall of the health problems by providing a booklet with each medical problem listed separately and having participants identify the number of the health problems. This method has been shown to decrease possible discomfort associated by identifying the problems by name (Kessler & Wethington, 1991). It should be noted that, at baseline, the NCS-1 survey asked participants about the presence or absence of only one painful medical condition (i.e., arthritis/rheumatism); however, no other pain-related disorder was assessed at baseline.

Health problem count at baseline.—For each health problem identified, a count of the number of these disorders was calculated. This count variable was used in the regression analyses to adjust, in part, for baseline medical conditions.

Pain severity at baseline.—If participants identified having one or more health problems, they were then asked: "How much pain do you experience as a result of your health problems?" Participants responded by using a 4-point Likert-type scale anchored at 1 (*none at all*) to 4 (*a lot*). Level of pain at baseline was controlled for in the analyses.

NCS-2 follow-up.—The follow-up NCS-2 survey assessed for some painful medical conditions.

Painful medical disorders.—At follow-up, participants were asked about their medical conditions. "The next few questions are about health problems you might have had at any time *since* (NCS-1 YEAR). Have you ever had any of the following conditions since (NCS-1 YEAR): arthritis or rheumatism (no = 0, yes = 1), chronic back or neck problems (no = 0, yes = 1), frequent or severe headaches (no = 0, yes = 1), any other chronic pain (no = 0, yes = 1)?" It is important to note that the pain-related disorders reported by the participants = (e.g., NCS-2) may have first occurred before the baseline NCS-1 was conducted and then persisted through the follow-up period. Or the disorder may have first occurred (e.g., new onset) during the 10-year follow-up period.

Painful medical disorders count.—The dependent measure in the regression analysis was the number of painful medical conditions that occurred during the 10-year follow-up period (e.g., between baseline and follow-up). The range for this count variable was 0 to 4. It is important to note that the dependent measure is *not* an assessment of the participant's experience of pain, but rather represents a sum of the number of self-reported pain-related related medical conditions.

Internal validity of the assessment of the pain disorders.—To obtain some measure of the internal validity of the assessment of the number of painful conditions, we examined the correlation between the number of painful medical conditions occurring over the last 10 years and a measure of the current (last 30 days) level of *discomfort* due to medical conditions. That is, in a separate section of the NCS-2, participants were asked questions about their health in the past 30 days, for example, "How often did you experience physical discomfort, such as pain, nausea, or dizziness in the past 30 days?" Responses were coded on a 4-point scale ranging from 1 (*all*) to 4 (*none of the time*). The correlation

between number of pain-related problems in the last 10 years and the measure of current discomfort in the past 30 days was 0.47 (N = 4981), p < .001.

Single item, self-report assessments of health clearly have psychometric limitations. Nonetheless, perceived health has been shown to provide an accurate gauge of physical health outcomes (Wu, 2013), to possess good reliability (Pettit, Kline, Gencoz, Gencoz, & Joiner, 2001), have good predictive validity (DeSalvo, Bloser, Reynolds, He, & Muntner, 2006; Schnittker, 2014) and have good agreement with physician diagnosis (see Bombak, 2013).

Data Analyses

First, we provide descriptive statistics for the sample as a whole. We then present a series of Poisson regression analyses, which were conducted to test the main effects model, moderation model, and mediation model described above.

Poisson regression analyses.—Poisson regression analyses are similar to regular multiple regression except that the dependent variable is an observed count that follows the Poisson distribution. Thus, the possible values of *Y (painful medical conditions)* are the non-negative integers (e.g., 0, 1, 2, 3, 4). Because count values are not typically normally distributed, standard linear regression analyses may produce biased results (Cameron & Trivedi, 1998; Coxe, West, & Aiken, 2009). Poisson regression is a special case of generalized linear modeling in which the natural log of Y is expressed as a linear function of predictors. Poisson analyses are often suggested for trauma-related research in which the outcome of interest is often a count of the number of incidents of behavior or number of specific problems occurring in a given time interval, such as the number of health problems (Gagnon, Doron-LaMarca, Bell, O'Farrell, & Taft, 2008).

Mediation analysis.—The role of the anxiety and mood disorders in mediating the relationship between ACEs and painful medical conditions was formally tested using bootstrap mediation analyses (Hayes & Scharkow, 2013; Preacher, 2015). The mediation model used in the current study took into consideration that both the mediator and the dependent measure were count variables. In the mediation model, the indirect effect was computed by multiplying the appropriate coefficients from the linear predictor components of the two Poisson regressions, as recommended by Preacher (2015) for generalized linear mediation models in which both the mediator (e.g., number of anxiety and mood disorders) and the outcome (number of painful medical conditions) are count variables. We used 5,000 bootstrap resamples to create bias-corrected confidence intervals. A 95% confidence interval (CI) that excluded zero indicated a statistically significant indirect effect.

Results

Demographics

The weighted population (N = 5001), by design, had an even distribution by gender. The mean age at follow-up was 43.03 (standard deviation [*SD*] = 10.5 years. Race was reported

as follows: Caucasian (75.5%), African American (11.6%), Hispanic (9.4%), and other (3.5 %). The average years of formal education was 12.8 (*SD* = 2.5) years.

Retrospective reports of ACEs.—The ACE variables, including frequency and severity ratings, are summarized in Table 1. The majority of participants reported never experiencing any verbal (51.3%), sexual (96.0%), or physical abuse (95.2%) in childhood. Among the participants, 21.8% reported early parental loss due to divorce, early parental death, or abandonment. Regarding family of origin income, participants were asked to report their family's income on a 5-pont Likert-type scale ranging from 1 (*a lot better off*) to 5 (*a lot worse off*). The distribution was skewed to the right such that a majority indicated that their status was "better off than most" (see Table 1). This may reflect the participants' bias toward perceiving their family as relatively better off than it was, or it may reflect an undersampling of those who lived in families with extremely low incomes. Table 1 also reports the mean symptom counts of each of the parental symptom counts (e.g., internalizing and externalizing).

The ACE simple count measure.—The simple ACE count score considers whether or not there was presence of a specific ACEs (yes = 1/no = 0). The simple ACE count could theoretically range from 0 to 9. However, the actual range was (0 to 7). The simple ACE score count was used in developing the mediation and moderation analyses model, and it was also used for descriptive purposes in the tables and figure. The distribution of the simple ACE count was as follows: 0 ACEs (41.5%), 1 ACEs (31.5%), 2 ACEs (14.5%), 3 ACEs (8.0%), 4+ ACEs (4.4%).

Psychiatric disorders at baseline.—Lifetime rates of each of the specific psychiatric disorder at baseline are as follows: major depression = 17.2%, bipolar disorder = 1.6%, GAD = 4.8%, social phobia = 13.5%, panic = 3.3%, and PTSD = 7.3%. The percentage of each psychiatric disorder associated with the simple ACEs count is described in Table 2. As shown in Table 2, there appears to be a graded relationship between the number of ACEs and each psychiatric disorder. Remarkable is the very high rate of major depression and PTSD among those with four or more ACEs (41.2% and 42.4%, respectively).

Additional covariates at baseline.—In the analyses, we also adjusted for health problems and pain severity ratings at baseline. Overall, 28.9% of the sample reported at baseline having 1 or more health problems (mean = 0.42; *SD* =.81). Baseline pain was assessed using a 4-point Likert-type scale ranging from 0 (*none at all*) to 3 (*a lot*). The mean baseline pain score was 0.3 (*SD* = .77).

NCS-2. Measures

Painful medical conditions at NCS-2 follow-up.—Participants were asked about the occurrence of painful medical conditions during the 10-year period (e.g., between NCS-1 and NCS-2).

The average number of painful medical conditions occurring during follow-up was .82 (*SD* = 1). Rates of the disorders were as follows: 23% arthritis or rheumatism, 25.9% back and neck problems, 21.9% frequent severe migraines or headaches, and 12.1% for "any other"

type of chronic pain. Similar to the association observed between the number of retrospective reports of ACEs and the number of baseline psychiatric disorders, there appears to be a graded relationship between number of retrospective reports of ACEs and the number of painful medical conditions obtained at follow-up (see Table 2).

Poisson Regression Analyses: Main Effects Model

Poisson regression analyses were conducted to examine the association of each specific ACE, each mood and anxiety disorder, with the number of painful medical conditions. The Poisson regression analyses and slopes are summarized in Table 3. Demographic characteristics were entered in the first model. With the exception of race, each of the demographic variables (e.g., female sex, older age, and fewer years of education) was associated with the number of painful medical conditions. In each additional model, we hold constant the variables included in each of the previous models.

In the second model, we entered the specific types of parental abuse (verbal, physical, sexual) and found that verbal and sexual abuse (but not physical) were associated with an increased number of painful medical conditions. In Model 3, we entered each of the other ACEs. With the exception of mother's externalizing symptoms, each parental pathology symptom count (e.g., father's externalizing and internalizing, and mother's internalizing symptoms) was associated with the number of painful medical conditions. Whereas early parental loss was associated with the number of painful medical conditions, family-of-origin income was unrelated. In Model 4, we entered the participant's number of baseline health conditions and baseline pain; both were associated with number of painful medical conditions at follow-up. It is of note that verbal abuse and sexual abuse remain significantly associated with number of painful medical conditions, even after controlling for each of the other ACEs and the participants' baseline health and pain levels.

In Model 5, holding constant variables included on previous steps, we entered each of the anxiety and mood disorders. Among the mood disorders, both depression and bipolar disorder were associated with pain-related medical conditions. Among the anxiety disorders, only PTSD (but not panic, GAD, or social phobia) was associated with the pain-related medical conditions. It should be noted that with the inclusion of these psychiatric disorders in Model 5, verbal and sexual abuse were no longer significant. Indeed, if the psychiatric disorders are mediators of the abuse–painful medical conditions association, then we would have expected, with the inclusion of the psychiatric disorders, that the association between the abuse variables and the number of painful medical conditions would weaken. Formal mediation analyses are conducted below to determine if statistically significant mediation has occurred.

Moderation Analyses

We expected that as the number of ACEs increased, so would the number of painful medical conditions. We expected that ACEs would have an effect on the number of painful medical conditions at both lower and higher levels of anxiety/mood disorder. Second, we expected the effect of ACEs on increasing painful medical conditions would be greater among participants with higher levels of anxiety/mood disorders compared to those with lower

levels. To test this hypothesis, we conducted a Poisson regression analyses, in which we included the covariates and the main effects of the number of ACEs, and the number of anxiety and mood disorders. We entered the interaction term (ACEs and mood/anxiety disorders) into the analyses. As expected, we found both the number of ACEs (B = .071, standard error [SE] = .010, p < .001, 95% CI [.052, .090]) and the number of mood/anxiety disorders (B = .138, SE = .017, p < .001, 95% CI [.105, .170]) were associated with an increase in painful medical conditions. Second, we found a significant *negative* interaction (B = −.038, SE = .008, p < .001, 95% CI [−.053, −.023]). To clarify the nature of the negative interaction between the psychiatric disorders and ACEs, we plotted the results (see Figure 1).

We had predicted that ACEs would have a greater effect on painful medical conditions among participants who had *higher* levels of anxiety/mood disorders compared to those with lower levels–this was not the case. Instead, we found that ACEs had a greater effect on increasing painful medical conditions at *lower levels* of anxiety/mood disorders. Figure 1 depicts the predicted count of painful medical conditions as a function of ACEs at four conditional values of mood/anxiety disorders (0–3). In interpreting Figure 1, it is important to note that both the count of mood/anxiety disorders and ACEs were skewed such that higher counts were relatively rare. About 99% of the sample reported 6 or fewer ACEs, and about 99% reported 3 or fewer mood/anxiety disorders. We plot prediction lines only for the bottom 99% of these distributions. In sum, whereas the effect of ACEs on painful conditions was positive overall, the effect was particularly strong among those reporting fewer anxiety and mood disorders.

Mediation Analyses

We also examined the mediating role of anxiety and mood disorders in the relationship between ACEs and painful medical conditions, while controlling for sex, age, education, race, and baseline health and pain. First, using Poisson regression as implemented in Mplus 7.4 (Muthén & Muthén, 1998–2016) we found that the simple count of summed ACEs was positively associated with the number of anxiety and mood disorders (B = .206, p < .001, 95% CI [0.187, 0.224]). Moreover, also using Poisson regression analyses anxiety and mood disorders were significantly associated with the number of painful medical conditions, controlling for ACEs (B = .109, p < .001, 95% CI [0.081, 0.138]). The direct effect of ACEs on painful medical conditions was also significant (B = .056, p < .001, 95% CI [0.038, 0.073]). Finally, the indirect effect of ACEs on painful medical conditions through anxiety and mood disorders was significant (indirect effect = .023, 95% bias-corrected bootstrap CI [0.017, 0.029]); however, with the inclusion of the mediator, the direct effect of ACEs on painful medical conditions remained significant. Thus, the analyses support the existence of an indirect effect of ACEs on painful medical conditions at follow-up via anxiety and mood disorders at baseline.

Discussion

In the current study, we examined the association between retrospective reports of ACEs and the development of a number of pain-related medical conditions (e.g., arthritis or

rheumatism, chronic back or neck problems, frequent or severe headaches, any other chronic pain) occurring over a 10-year period. We also examined the mediating and moderating role of mood and anxiety disorders in the ACEs-painful medical conditions associations.

In the main effects model, we found that older age, female sex, lower education, baseline health, and baseline pain levels were associated with the number of pain-related medical conditions at follow-up. We also found several specific ACEs to be associated with the number of pain-related medical conditions. These ACEs included parental verbal abuse, sexual abuse, mother's internalizing, father's externalizing and internalizing symptoms, and early parental loss. Among the baseline lifetime anxiety disorders, only PTSD (but not GAD, social phobia, or panic disorder) was associated with painful medical conditions. However, both baseline lifetime mood disorders (i.e., depression and bipolar disorder) were associated with the number of pain-related medical conditions.

Mediation and moderation analyses were conducted to further elucidate the role of mood and anxiety disorders on the association between ACEs and painful medical conditions. As predicted, we found the mediation model to indicate that the number of anxiety and mood disorders partially mediated the relationship between ACEs and the number of painful medical conditions. That is, ACEs contributed to participants' lifetime anxiety and mood disorders, and these disorders, in turn, contributed to the development of pain-related medical conditions.

Analyses also revealed an interaction (e.g., moderation) between the number of ACEs and number of anxiety and mood disorders in its association with the number of pain-related conditions. First, as expected, we found that participants with a greater number of mood/anxiety disorders and with higher levels of ACEs had more painful medical conditions, and participants with lower levels of ACEs and a lower number of anxiety/mood disorders had fewer painful medical conditions. Our analyses also indicated that anxiety/mood disorders had an effect on increasing painful medical conditions at both high and low levels of ACEs. However, inconsistent with predictions, we determined that the effect of ACEs on increasing the number of painful medical conditions was greater among those with lower levels of anxiety and mood disorders, compared to higher levels. This unexpected finding will be discussed further below.

ACEs, Painful Medical Conditions, and Aging

In the current study, we found that retrospective reports of ACEs, assessed at baseline, were associated with the number of painful medical conditions occurring during the 10-year follow-up period. The conditions included arthritis /rheumatism, severe and/or frequent headaches, back or neck pain, or any other pain-related medical condition. Our findings are consistent with past studies finding an association between ACEs and painful medical disorders.

Past research has confirmed an association between ACEs and the painful medical conditions examined in the current study. ACEs have been found to be associated with the subsequent development of arthritis and rheumatism (Baldassari, Cleveland, & Callahan, 2013) and an increased risk of neck and back pain (Scott et al., 2011). ACEs have been

found to be associated with the development of headaches (Tietjen, Karmakar, Elhai, & Amialchuk, 2016) and transformation of moderate tension headaches to more severe migraines (Tietjen et al., 2010). There is a growing scientific literature regarding the neurobiological effects of child abuse on brain function and structure that suggest a possible role of early life stress in the pathogenesis of migraine (Tietjen et al., 2015).

We examined the association between ACEs and the number of painful medical conditions over a 10-year follow-period. Most pain-related disorders tend to increase with age. Indeed, age is the most important risk factor for the development of chronic rheumatoid arthritis (Chalan et al., 2015). The prevalence of back and neck pain has also been found to increase with age. For example, using longitudinal data from the Medical Expenditures Panel Survey (N = 71 838), researchers reported that over the 7-year follow-up period, the prevalence of back pain increased by 29% and chronic back pain increased by 64% (Smith et al., 2013). Whereas many pain-related medical conditions are associated with aging, headaches are not. Indeed, the prevalence of headache decreases with age; nonetheless, headache is still ranked as one of the most frequent complaints in the elderly (Tanganelli, 2010).

Mechanisms Linking ACEs, Anxiety, Mood Disorders, and Painful Medical Conditions

There are fundamental changes in the developmental trajectory of biological, psychological, and behavioral processes that result from early stressors which exert influence throughout the lifespan (Sachs-Ericsson, Rushing, Stanley, & Sheffler, 2016). First, it may be the case that ACEs affect some of the same neurological, biological, and psychological mechanisms that influence mood and anxiety disorders as well as pain-related medical conditions (Nemeroff, 2016). In particular, chronic stressors affect the HPA stress response, influencing cortisol patterns and the autoimmune system. Dysregulation of the HPA and autoimmune functioning may, in turn, be the neurological substrate linking ACEs to mood and anxiety disorders (Heim et al., 2010) and painful medical conditions later in adulthood (Blackburn-Munro & Blackburn-Munro, 2001; Denk, McMahon, & Tracey, 2014; Slavich & Irwin, 2014; Weissbecker, Floyd, Dedert, Salmon, & Sephton, 2006; Yeung, Davis, & Ciaramitaro, 2015).

How Childhood Stressors Impact Stress and Health in Adulthood

How is it that childhood adversities affect health decades later? Unfortunately, individuals exposed to ACEs are more likely to experience subsequent negative life events in adulthood. Indeed, childhood emotional abuse prospectively predicted greater stress generation (Liu, Choi, Boland, Mastin, & Alloy, 2013). Second, individuals who experienced earlier childhood sexual or physical abuse appear to have a more intense response to such stressors (Cromer & Sachs-Ericsson, 2006), thought to be driven, in part, by the dysregulation of the HPA stress response.

The “sensitization” hypothesis posits that prior exposure to any trauma sensitizes individuals to respond more intensely to subsequent stressors (Resnick, Yehuda, Pitman, & Foy, 1995; Yehuda et al., 1995). The mechanism underlying this process is an altered neurobiology that occurs after initial exposure to earlier stressors (Christine Heim, Ehlert, & Hellhammer, 2000; Christine Heim, Newport, Bonsall, Miller, & Nemeroff, 2001), the effects of which

are exacerbated when stressors occur in midlife or later adulthood. Thus, typical stressors occurring in midlife (e.g., role changes, employment difficulties, increased health problems, and family stressors such as marriage or divorce, problems with raising children; Aldwin & Levenson, 2001) may increase stress and deplete resources. For individuals who have experienced ACEs, such challenges may be substantially more difficult. Miller and colleagues (Miller, Chen, & Parker, 2011) suggest that over the life course, the proinflammatory tendencies associated with ACEs drive inflammation and the pathogenic systems that ultimately lead to chronic medical diseases and pain-related conditions during aging. Chronic inflammation may be a common cause of multiple age-related diseases (Singh & Newman, 2011).

Family Environment, Mood and Anxiety Disorders, and Painful Medical Conditions

Our measure of ACEs also included indices of parental psychopathology. In our analyses, in which we entered each specific ACE, we found that father's internalizing and externalizing symptoms and mother's internalizing symptoms contributed to the participant's pain-related medical conditions. Additionally, the mediation model demonstrated that the summed ACE measure (which included the parental internalizing and externalizing psychopathology) contributed to participants' baseline mood and anxiety disorders. These mood and anxiety disorders, in turn, contributed to the number of painful medical conditions. There are several factors that may explain these associations.

First, mood and anxiety are heritable disorders (Hettema, Neale, & Kendler, 2001; Sullivan, Neale, & Kendler, 2000). Thus, parental pathology (one indicator of ACEs) likely contributed to participants' risk for the anxiety and mood disorders. Moreover, parental pathology also contributes to a dysfunctional family environment (Berg-Nielsen, Vikan, & Dahl, 2002). Parents who score high on measures of pathology display a more forceful and negative parenting style (Kochanska, Aksan, & Nichols, 2003) and provide lower parental care (Yehuda, Halligan, & Bierer, 2002). The effects of such dysfunctional parenting are associated with a range of negative psychological outcomes across developmental periods (Berg-Nielsen et al., 2002).

ACEs, and in particular parental pathology and childhood abuse, have long-term effects on the development of cognitive styles that contribute to the development of anxiety and mood disorders (Gibb, Abramson, & Alloy, 2004; Rose & Abramson, 1992; Sachs-Ericsson et al., 2006). Early parental abuse is thought to increase hypervigilance to threat and negatively affect cognitive processes related to the development of anxiety and pain (Davis et al., 2005; Maniglio, 2013). Cognitive distortions may play a direct role in pain perception by lowering thresholds for labeling painful stimuli as noxious (Arnow, Hart, Hayward, Dea, & Barr-Taylor, 2000; Asmundson & Katz, 2008; Drossman, 1994; Scarinci, McDonald-Haile, Bradley, & Richter, 1994). Catastrophic cognitions about pain may worsen the subjective experience of pain (Asmundson & Katz, 2009; Marshall, Miles, & Stewart, 2010; Ocañez, McHugh, & Otto, 2010).

Dysfunctional parenting is also likely to lead the child to develop poorer coping skills that make him or her more vulnerable to subsequent stressors. For example, in one study, child maltreatment was found to be an important risk factor for adverse health outcomes in later

life, with current stress and poor coping strategies influencing this relationship (Hager & Runtz, 2012). Indeed, as described below, differences in the effect of ACEs on coping resources may potentially explain our unexpected moderation results. Specifically, inconsistent with predictions, we determined through moderation analyses the effect of ACEs on increasing the number of painful medical conditions was greater among participants at lower levels of mood and anxiety disorders compared to those with higher levels.

Mediation, Moderation, and Reserve Capacity

Our findings indicate that anxiety and mood disorders act as both mediators and moderators in the relationship between ACEs and painful medical disorders, which, as reviewed above, is due to a multitude of risk factors that work in tandem across the lifespan. The model of reserve capacity offers additional insight into how these complex processes may evolve over time (Gallo & Matthews, 2003). Researchers have demonstrated that individuals who experience early adversities may develop less effective coping strategies and limited reserve capacity (i.e., resilient psychological, emotional, and cognitive resources). The model posits that throughout life, people accumulate reserve capacity that allows them to endure adverse circumstances. When difficult circumstances become taxing beyond existing coping resources and reserve capacity, then diminished well-being can occur (Grundy, 2006; Piazza, Charles, & Almeida, 2007).

Consistent with the mediation results, individuals with a history of ACEs may have fewer coping resources and lower reserve capacity needed to manage life stressors, placing them at risk for developing an anxiety or mood disorder. The anxiety and mood disorders, in turn, may further deplete the limited reserve capacity, making an individual more prone to painful medical conditions. Moderation analyses also revealed a significant interaction between ACEs and anxiety/mood disorders in the prediction of painful medical conditions. However, we determined that that the effect of ACEs on the number of painful medical conditions was even stronger for participants reporting fewer anxiety/mood disorders compared to those reporting more anxiety/mood disorders. To put it another way, for those with high levels of ACEs, the subsequent development of mood/anxiety disorders contributed little to increasing the number of painful medical conditions. It may be the case that individuals who experienced high levels of ACEs have limited reserve capacity from which to draw - leading them to be more susceptible to painful medical conditions regardless of the presence or absence of anxiety/mood disorders. Thus, for those with high levels of ACEs, there is some ceiling effect such that the co-occurrence of mood/anxiety disorders does not substantially contribute to increased painful medical conditions.

In contrast, people with low levels of ACEs may have developed greater reserve capacity over time compared to those exposed to higher levels of ACEs. However, when these individuals experience anxiety or mood disorders, their reserve capacity then becomes depleted, making the association between the anxiety/mood disorders and painful medical conditions stronger. Thus, the effect of anxiety/mood disorders on painful medical conditions is related to one’s existing coping strategies and reserve capacity, which are challenged at different levels depending on the number of ACEs they have experienced.

Strengths and Limitations

The current investigation is among one of the very few prospective epidemiological studies that examines the mediating and moderating roles of mood and anxiety disorders in the association of retrospectively reported ACEs and the subsequent occurrence of painful medical conditions. Further, the current study used an inclusive definition of ACEs (e.g., childhood sexual, physical, and verbal abuse; parental psychopathology; early parental loss) as well as valid and reliable measures of DSM-derived diagnoses.

Limitations of the current study are as follows. First, the study relied on retrospective self-reports of participants' abuse. Given that the abuse occurred before age 15, respondents were reporting on events that happened, on average, approximately 20–30 years prior. The long period of time between the event and the assessment of the event may affect the reliability of the reports. In this regard, a vast majority of studies examining the consequences of childhood adversities on adult outcomes have used retrospective self-report measures (Kalmakis & Chandler, 2015). Although using such measures may have threatened study reliability through recall bias, retrospective responses of ACEs have been found to be generally stable over time (Dube et al., 2004). Using meta-analyses with sophisticated methods to identify the reliably and validity of such measures, researchers have documented that false positives are rare, although there are significant concerns regarding false negatives (Hardt & Rutter, 2004). Indeed, in the current study, there appeared to be low rates of retrospective reports of physical and sexual abuse. Thus, the probability of underreporting of abuse in the current study must be considered in light of the findings (e.g., it is likely that a number of participants who actually had past abuse did not report it in this survey).

It may be the case that childhood abuse experiences may be more salient to those who were most affected by the abuse (e.g., those experiencing mental health problems or painful medical conditions). Thus, those least affected by the abuse may be more likely to underreport abuse experiences. This may have enhanced the apparent relationship between abuse and the painful medical disorders examined in the current study. Moreover, whereas the mediation model conceptualizes that the retrospective reports of abuse predict the psychiatric disorders, it must be remembered that the abuse variables and psychiatric disorders were assessed at the same time. Thus, the temporal order cannot be clearly established.

In the current study, we did not examine the association between baseline pain conditions and their contribution to the subsequent development of mood and anxiety disorders. There is evidence of bidirectionality of the link between mood/anxiety disorders and pain. Indeed, pain disorders have also been found to increase risk of mood and anxiety disorders (Bair et al., 2013; Fishbain, Cutler, Rosomoff, & Rosomoff, 1997; Gerrits et al., 2012; Lerman, Rudich, Brill, Shalev, & Shahar, 2015; Simons, Elman, & Borsook, 2014). They may also influence one another in some mutually maintaining way or some third factor (e.g., a common predisposition or a shared environmental event) may increase vulnerability to both (Asmundson & Katz, 2009; Norton & Asmundson, 2003).

An additional limitation of the current study is that we have no measure of HPA axis functioning or autoimmune functioning. Thus, we cannot evaluate directly the extent to

which HPA and autoimmune dysregulation is associated with the relationships among ACEs, mood and anxiety disorders, and pain-related medical conditions. Further, whereas early trauma may influence the development of avoidant, less effective coping skills (Hager & Runtz, 2012), we have no measure of coping styles or any indices of reserve capacity to directly test this hypothesis. Finally, we should note that our measure of painful medical conditions was a simple count of a limited number of painful medical conditions. A more inclusive and nuanced measure of painful medical conditions and level of pain associated with the conditions may have allowed us to better understand the complex associations examined in the current study.

As noted in the manuscript, participants' reports of family-of-origin income were skewed such that most reported having better financial status than others in childhood. This may indicate that there was not an adequate sampling of individuals with lower income in childhood, or it may be a bias toward perceiving one's circumstances as better than they actually were. Indeed, family-of-origin income was not related to the number of painful medical conditions, though many other studies have found such associations. Thus, bias in reporting may have affected the results.

Directions for Future Research

Building on the aforementioned strengths and limitations, several recommendations are made for future research in this area. Given the pernicious effects of ACEs across mental (e.g., mood, anxiety) and physical (e.g., painful medical conditions) domains, it is important to build on our current knowledge of the etiology, course, and treatment of disorders influenced by ACEs. Individuals exposed to ACEs who also have psychiatric and medical disorders appear to respond less well than others to traditional psychotherapy and pharmacological treatments, and thus Nemeroff (2016) suggests that such individuals may comprise a unique endophenotype that requires novel treatment.

Further, investigation of the role of the HPA system in response to childhood stress may elucidate the neural, biological, and psychological pathways between ACEs and later psychopathology and pain disorders (Nemeroff, 2016). In this regard, greater understanding of the neurobiological substrates that influence chronic inflammation may also provide a point of intervention through pharmacological and behavioral treatments that better regulate the stress response (Walker, Kavelaars, Heijnen, & Dantzer, 2013). As others have noted (Leonard, 2015; Verma, Sheikh, & Ahmed, 2014), by understanding the critical role that chronic arousal of the HPA axis plays in the development of mood and anxiety disorders and pain, novel pharmacological and psychotherapeutic approaches may emerge. Further, it may be possible to develop psychotherapeutic treatments to increase effective coping and build the individual's potential for resilience in the face of future adversities. Such exploration may lead to strategies that thwart the trajectory from ACEs to adult mood and anxiety disorders and to painful medical conditions.

Conclusion

The current study demonstrates that retrospective reports of ACEs and lifetime mood and anxiety disorders independently contribute to the occurrence of painful medical conditions.

We also found that ACEs increased the risk mood and anxiety disorders, and, in turn, these disorders appear to influence the development of painful medical conditions. Although ACEs contributed to a greater number of painful conditions regardless of the level of mood and anxiety disorders, the effect was more pronounced for individuals with lower levels of mood and anxiety disorders. Taken together, findings indicate the ACEs have potent effects on the development of pain-related medical conditions, and mood and anxiety disorders may, in part, account for this link.

Acknowledgments

Jennifer R. Piazza's research is funded by National Institutes of Health, National Institute on Aging (R03 AG047955).

References

Afifi TO , Enns MW , Cox BJ , Asmundson GJ , Stein MB , & Sareen J (2008). Population attributable fractions of psychiatric disorders and suicide ideation and attempts associated with adverse childhood experiences. American Journal of Public Health, 98(5), 946–952. 10.2105/AJPH.2007.120253 [PubMed: 18381992]

Anda RF , Felitti VJ , Bremner JD , Walker JD , Whitfield C , Perry BD , … Giles WH (2006). The enduring effects of abuse and related adverse experiences in childhood. European Archives of Psychiatry and Clinical Neuroscience, 256(3), 174–186. 10.1007/s00406-005-0624-4 [PubMed: 16311898]

Andreasen NC , Endicott J , Spitzer RL , & Winokur G (1977). The family history method using diagnostic criteria: Reliability and validity. Archives of General Psychiatry, 34(10), 1229–1235. 10.1001/archpsyc.1977.01770220111013 [PubMed: 911222]

APA. (1987). DSM-III-R: Diagnostic and Statistical Manual of Mental Disorders. (III, Revised ed.). Washington, D.C.: American Psychiatric Association.

Arnow B , Hart S , Hayward C , Dea R , & Barr Taylor C (2000). Severity of child maltreatment, pain complaints and medical utilization among women. Journal of Psychiatric Research, 34(6), 413–421. 10.1016/s0022-3956(00)00037-6 [PubMed: 11165309]

Asmundson GJG , & Katz J (2008). Understanding pain and posttraumatic stress disorder comorbidity: Do pathological responses to trauma alter the perception of pain? Pain, 138(2), 247–249. 10.1016/j.pain.2008.06.020 [PubMed: 18684567]

Asmundson GJG , & Katz J (2009). Understanding the co-occurrence of anxiety disorders and chronic pain: state-of-the-art. Depression and Anxiety, 26(10), 888–901. 10.1002/da.20600 [PubMed: 19691031]

Bailey BE , Freedenfeld RN , Kiser RS , & Gatchel RJ (2003). Lifetime physical and sexual abuse in chronic pain patients: Psychosocial correlates and treatment outcomes. Disability and Rehabilitation, 25(7), 331–342. 10.1080/0963828021000056866 [PubMed: 12745957]

Bair MJ , Poleshuck EL , Wu J , Krebs EK , Damush TM , Tu W , & Kroenke K (2013). Anxiety but not social stressors predict 12-month depression and pain severity. The Clinical Journal of Pain, 29(2), 95–101. 10.1097/AJP.0b013e3182652ee9 [PubMed: 23183264]

Baldassari AR , Cleveland RJ , & Callahan LF (2013). Independent influences of current and childhood socioeconomic status on health outcomes in a North Carolina family practice sample of arthritis patients. Arthritis Care & Research, 65(8), 1334–1342. 10.1002/acr.21969 [PubMed: 23401367]

Baron RM , & Kenny DA (1986). The moderator-mediator variable distinction in social psychological research: Conceptual, strategic, and statistical considerations. Journal of Personality & Social Psychology, 51, 1173–1182. 10.1037/0022-3514.51.6.1173 [PubMed: 3806354]

Berg-Nielsen TS , Vikan A , & Dahl AA (2002). Parenting related to child and parental psychopathology: A descriptive review of the literature. Clinical Child Psychology and Psychiatry, 7(4), 529–552. 10.1177/1359104502007004006

Björkenstam E , H. A , Mittendorfer-Rutz E , Vinnerljung B , Hallqvist J , & Ljung R (2013). Multi-exposure and clustering of adverse childhood experiences, socioeconomic differences and psychotropic medication in young adults. PLoS ONE 8(1), e53551 10.1371/journal.pone.0053551 [PubMed: 23341951]

Blackburn-Munro G , & Blackburn-Munro R (2001). Chronic pain, chronic stress and depression: Coincidence or consequence? Journal of Neuroendocrinology, 13(12), 1009–1023. 10.1046/j.0007-1331.2001.00727.x [PubMed: 11722697]

Bombak AE (2013). Self-rated health and public health: A critical perspective. Frontiers in Public Health, 1(15). 10.3389/fpubh.2013.00015

Brown J , Berenson K , & Cohen P (2005). Documented and self-reported child abuse and adult pain in a community sample. The Clinical Journal of Pain, 21(5), 374–377. 10.1097/01.ajp.0000149797.16370.dc [PubMed: 16093742]

Cameron AC , & Trivedi PK (1998). Regression analysis of count data. New York: Cambridge University Press.

Aldwin Carolyn M. , & Levenson MR (2001). Stress, coping, and health at mid-life: A developmental perspective In Lachman ME (Ed.), The handbook of midlife development. New York: Wiley.

Chalan P , van den Berg A , Kroesen B-J , Brouwer L , & Boots A (2015). Rheumatoid arthritis, immunosenescence and the hallmarks of aging. Current Aging Science, 8(2), 131–146. 10.2174/1874609808666150727110744 [PubMed: 26212057]

Clark C , Caldwell T , Power C , & Stansfeld SA (2010). Does the influence of childhood adversity on psychopathology persist across the lifecourse? A 45-year prospective epidemiologic study. Annals of Epidemiology, 20(5), 385–394. 10.1016/j.annepidem.2010.02.008 [PubMed: 20382340]

Cougle JR , Timpano KR , Sachs-Ericsson N , Keough ME , & Riccardi CJ (2010). Examining the unique relationships between anxiety disorders and childhood physical and sexual abuse in the National Comorbidity Survey-Replication. Psychiatry Research, 177(1–2), 150–155. 10.1016/j.psychres.2009.03.008 [PubMed: 20381878]

Coxe S , West SG , & Aiken LS (2009). The analysis of count data: A gentle introduction to Poisson regression and its alternatives. Journal of Personality Assessment, 91(2), 121–136. 10.1080/00223890802634175 [PubMed: 19205933]

Cromer KR , & Sachs-Ericsson N (2006). The association between childhood abuse, PTSD, and the occurrence of adult health problems: Moderation via current life stress. Journal of Trauma Stress, 19(6), 967–971. 10.1002/jts.20168

Davis DA , Luecken LJ , & Zautra AJ (2005). Are reports of childhood abuse related to the experience of chronic pain in adulthood. The Clinical Journal of Pain, 21(5), 398–405. 10.1097/01.ajp.0000149795.08746.31 [PubMed: 16093745]

Denk F , McMahon SB , & Tracey I (2014). Pain vulnerability: A neurobiological perspective. Nature Neuroscience, 17(2), 192–200. 10.1038/nn.3628 [PubMed: 24473267]

DeSalvo KB , Bloser N , Reynolds K , He J , & Muntner P (2006). Mortality prediction with a single general self-rated health question: A meta-analysis. Journal of General Internal Medicine, 21(3), 267– 275. 10.1111/j.1525-1497.2005.00291.x [PubMed: 16336622]

Draper B , Pfaff JJ , Pirkis J , Snowdon J , Lautenschlager NT , Wilson I , & Almeida OP (2008). Long-term effects of childhood abuse on the quality of life and health of older people: results from the Depression and Early Prevention of Suicide in General Practice Project. Journal of the American Geriatrics Society, 56(2), 262–271. 10.1111/j.1532-5415.2007.01537.x [PubMed: 18031482]

Drossman DA (1994). Physical and sexual abuse and gastrointestinal illness: What is the link? American Journal of Medicine, 97(2), 105–107. 10.1016/0002-9343(94)90019-1 [PubMed: 8059775]

Dube SR , Fairweather D , Pearson WS , Felitti VJ , Anda RF , & Croft JB (2009). Cumulative childhood stress and autoimmune diseases in adults. Psychosomatic Medicine, 71(2), 243–250. 10.1097/PSY.0b013e3181907888 [PubMed: 19188532]

Dube SR , Felitti VJ , Dong M , Chapman DP , Giles WH , & Anda RF (2003). Childhood abuse, neglect, and household dysfunction and the risk of illicit drug use: The Adverse Childhood Experiences Study. Pediatrics, 111(3), 564–572. 10.1542/peds.111.3.564 [PubMed: 12612237]

Edwards VJ , Holden GW , Felitti VJ , & Anda RF (2003). Relationship between multiple forms of childhood maltreatment and adult mental health in community respondents: Results from the adverse childhood experiences study. American Journal of Psychiatry, 160(8), 1453–1460. 10.1176/appi.ajp.160.8.1453 [PubMed: 12900308]

Felitti VJ , Anda RF , Nordenberg D , Williamson DF , Spitz AM , Edwards V , & Marks JS (1998). Relationship of childhood abuse and household dysfunction to many of the leading causes of death in adults. The Adverse Childhood Experiences (ACE) Study. American Journal of Preventative Medicine, 14, 245–258. 10.1016/s0749-3797(98)00017-8

Fishbain D , Cutler R , Rosomoff H , & Rosomoff R (1997). Chronic pain-associated depression: antecedent or consequence of chronic pain? A review. The Clinical Journal of Pain, 13(2), 116–137. 10.1097/00002508-199706000-00006 [PubMed: 9186019]

Gagliese L (2009). Pain and aging: The emergence of a new subfield of pain research. The Journal of Pain, 10(4), 343–353. 10.1016/j.jpain.2008.10.013 [PubMed: 19327641]

Gagnon DR , Doron-LaMarca S , Bell M , O'Farrell TJ , & Taft CT (2008). Poisson regression for modeling count and frequency outcomes in trauma research. Journal of Traumatic Stress, 21(5), 448–454. 10.1002/jts.20359 [PubMed: 18956443]

Gallo LC (2009). The Reserve Capacity Model as a framework for understanding psychosocial factors in health disparities. Applied Psychology: Health and Well-Being, 1(1), 62–72. 10.1111/j.1758-0854.2008.01000.x

Gallo LC , & Matthews KA (2003). Understanding the association between socioeconomic status and physical health: Do negative emotions play a role? Psychological Bulletin, 129(1), 10–51. 10.1037/0033-2909.129.1.10 [PubMed: 12555793]

Gerrits MMJG , Vogelzangs N , van Oppen P , van Marwijk HWJ , van der Horst H , & Penninx BWJH (2012). Impact of pain on the course of depressive and anxiety disorders. Pain, 153(2), 429–436. 10.1016/j.pain.2011.11.001 [PubMed: 22154919]

Gibb BE , Abramson LY , & Alloy LB (2004). Emotional maltreatment from parents, verbal peer victimization, and cognitive vulnerability to depression. Cognitive Therapy and Research, 28(1), 1–21. 10.1023/b:cotr.0000016927.18027.c2

Glaser D (2000). Child abuse and neglect and the brain: A review. The Journal of Child Psychology and Psychiatry and Allied Disciplines, 41(1), 97–116. 10.1111/1469-7610.00551

Gonzalez A , Boyle MH , Kyu HH , Georgiades K , Duncan L , & MacMillan HL (2012). Childhood and family influences on depression, chronic physical conditions, and their comorbidity: Findings from the Ontario Child Health Study. Journal of Psychiatric Research, 46(11), 1475–1482. 10.1016/j.jpsychires.2012.08.004 [PubMed: 22959202]

Green CR , Flowe-Valencia H , Rosenblum L , & Tait AR (2001). The role of childhood and adulthood abuse among women presenting for chronic pain management. The Clinical Journal of Pain, 17(4), 359–364. 10.1097/00002508-200112000-00011 [PubMed: 11783817]

Green J , McLaughlin KA , Berglund PA , Gruber MJ , Sampson NA , Zaslavsky AM , & Kessler RC (2010). Childhood adversities and adult psychiatric disorders in the National Comorbidity Survey Replication I: Associations with first onset of DSM-IV disorders. Archives of General Psychiatry, 67(2), 113–123. 10.1001/archgenpsychiatry.2009.186 [PubMed: 20124111]

Grundy E (2006). Ageing and vulnerable elderly people. European perspective. Ageing & Society, 26, 105–134. 10.1017/s0144686X05004484

Gunnar MR , & Vazquez DM (2001). Low cortisol and a flattening of expected daytime rhythm:Potential indices of risk in human development. Developmental Psychopathology, 13(3), 515–538. 10.1017/s0954579401003066

Hager AD , & Runtz MG (2012). Physical and psychological maltreatment in childhood and later health problems in women: An exploratory investigation of the roles of perceived stress and coping strategies. Child Abuse & Neglect, 36(5), 393–403. 10.1016/j.chiabu.2012.02.002 [PubMed: 22609072]

Hardt J , & Rutter M (2004). Validity of adult retrospective reports of adverse childhood experiences: Review of the evidence. Journal of Child Psychology and Psychiatry, 45(2), 260–273. 10.1111/j.1469-7610.2004.00218.x [PubMed: 14982240]

Hayes AF , & Scharkow M (2013). The relative trustworthiness of inferential tests of the indirect effect in statistical mediation analysis: Does method really matter? Psychological Science, 24(10), 1918–1927. 10.1177/0956797613480187 [PubMed: 23955356]

Heim C , Ehlert U , & Hellhammer DH (2000). The potential role of hypocortisolism in the pathophysiology of stress-related bodily disorders. Psychoneuroendocrinology, 25(1), 1–35. 10.1016/s0306-4530(99)00035-9 [PubMed: 10633533]

Heim C , & Nemeroff CB (2002). Neurobiology of early life stress: Clinical studies. Seminar in Clinical Neuropsychiatry, 7, 147–159. 10.1053/scnp.2002.33127

Heim C , Newport DJ , Bonsall R , Miller AH , & Nemeroff CB (2001). Altered pituitary-adrenal axis responses to provocative challenge tests in adult survivors of childhood abuse. American Journal of Psychiatry, 158(4), 575–581. 10.1176/appi.ajp.158.4.575 [PubMed: 11282691]

Heim C , Newport DJ , Mletzko T , Miller AH , & Nemeroff CB (2008). The link between childhood trauma and depression: Insights from HPA axis studies in humans. Psychoneuroendocrinology, 33(6), 693–710. 10.1016/j.psyneuen.2008.03.008 [PubMed: 18602762]

Heim C , Shugart M , Craighead WE , & Nemeroff CB (2010). Neurobiological and psychiatric consequences of child abuse and neglect. Developmental Psychobiology, 52(7), 671–690. 10.1002/dev.20494 [PubMed: 20882586]

Hettema JM , Neale MC , & Kendler KS (2001). A review and meta-analysis of the genetic epidemiology of anxiety disorders. American Journal of Psychiatry, 158(10), 1568–1578. 10.1176/appi.ajp.158.10.1568 [PubMed: 11578982]

Irish L , Kobayashi I , & Delahanty DL (2010). Long-term physical health consequences of childhood sexual abuse: A meta-analytic review. Journal of Pediatric Psychology, 35(5), 450–461. 10.1093/jpepsy/jsp118 [PubMed: 20022919]

Janca A , Robins LN , Cottler LB , & Early TS . (1992). Clinical observation of assessment using the Composite International Diagnostic Interview (CIDI). An analysis of the CIDI Field Trials–Wave II at the St Louis site. The British Journal of Psychiatry, 160(6), 815–818. 10.1192/bjp.160.6.815 [PubMed: 1617365]

Kalmakis KA , & Chandler GE (2015). Health consequences of adverse childhood experiences: A systematic review. Journal of the American Association of Nurse Practitioners, 27(8), 457–465. 10.1002/2327-6924.12215 [PubMed: 25755161]

Kessler R (1994). The National Comorbidity Survey of the United States. International Review of Psychiatry, 6, 365–376. 10.3109/09540269409023274

Kessler R (2013). National Comorbidity Survey: Re-interview (NCS-2), 2001–2002 [Restricted-Use]. 10.3886/ICPSR30921.v1

Kessler RC , Calabrese JR , Farley PA , Gruber MJ , Jewell MA , Katon W , … Wittchen HU (2013). Composite International Diagnostic Interview screening scales for DSM-IV anxiety and mood disorders. Psychological Medicine, 43(8), 1625–1637. doi:10.1017/s0033291712002334 [PubMed: 23075829]

Kessler R , McGonagle K , Zhao S , Nelson C , Hughes M , Eshleman S , … Kendler K (1994). Lifetime and 12-month prevalence of DSM-III-R psychiatric disorders in the United States: Results from the National Comorbidity Survey. Archives of General Psychiatry, 51(1), 8–19. 10.1001/archpsyc.1994.03950010008002 [PubMed: 8279933]

Kessler RC , Sonnega A , Bromet E , Hughes M , & Nelson CB (1995). Posttraumatic stress disorder in the National Comorbidity Survey. Archives of General Psychiatry, 52(12), 1048–1060. 10.1001/archpsyc.1995.03950240066012 [PubMed: 7492257]

Kessler RC , Sonnega A , Bromet E , Hughes M , Nelson CB , & Breslau N (1999). Epidemiological risk factors for trauma and PTSD In Yehuda R (Ed.), Risk factors for post traumatic stress disorder (pp. 23–59). Washington, DC: American Psychiatric Association Press.

Kessler RC , Stang PE , Wittchen H-U , Ustun TB , Roy-Burne PP , & Walters EE (1998). Lifetime panic-depression comorbidity in the National Comorbidity Survey. Archives of General Psychiatry, 55(9), 801–808. 10.1001/archpsyc.55.9.801 [PubMed: 9736006]

Kessler RC , & Walters E (2003). The National Comorbidity Survey In Ming MT , & Tsuang T (Ed.),Textbook in psychiatric epidemiology (2nd ed., pp. 343–362).

Kessler RC , & Wethington E (1991). The reliability of life event reports in a community survey. Psychological Medicine, 21, 723–738. 10.1017/s0033291700022364 [PubMed: 1946861]

Kessler RC , Wittchen H-U , Abelson J , & Zhao S (2000). Methodological issues in assessing psychiatric disorders with self-reports In Stone AA , Turrkan CA , Bachrach CA , Kurtzman HS , & Cain VS (Ed.), The science of self-reports: Implications for research and practice (pp. 229–255). New Jersey: Lawrence Erlbaum Associates.

Kochanska G , Aksan N , & Nichols KE (2003). Maternal power assertion in discipline and moral discourse contexts: Commonalities, differences, and implications for children's moral conduct and cognition. Developmental Psychology, 39(6), 949–963. 10.1037/0012-1649.39.6.949 [PubMed: 14584977]

Leonard BE (2015). Pain, depression and inflammation: Are interconnected causative factors involved? In Finn DP & Leonard BE (Eds.), Pain in psychiatric disorders (Vol. 30, pp. 22–35). Basel: Karger.

Lerman SF , Rudich Z , Brill S , Shalev H , & Shahar G (2015). Longitudinal associations between depression, anxiety, pain, and pain-related disability in chronic pain patients. Psychosomatic Medicine, 77(3), 333–341. 10.1097/psy.0000000000000158 [PubMed: 25849129]

Leserman J (2005). Sexual abuse history: Prevalence, health effects, mediators, and psychological treatment. Psychosomatic Medicine, 67(6), 906–915. 10.1097/01.psy.0000188405.54425.20 [PubMed: 16314595]

Lindert J , von Ehrenstein O , Grashow R , Gal G , Braehler E , & Weisskopf M (2014). Sexual and physical abuse in childhood is associated with depression and anxiety over the life course: Systematic review and meta-analysis. International Journal of Public Health, 59(2), 359–372. 10.1007/s00038-013-0519-5 [PubMed: 24122075]

Liu RT , Choi JY , Boland EM , Mastin BM , & Alloy LB (2013). Childhood abuse and stress generation: The mediational effect of depressogenic cognitive styles. Psychiatry Research, 206(2–3), 217–222. 10.1016/j.psychres.2012.12.001 [PubMed: 23273609]

Liu RT , Jager-Hyman S , Wagner CA , Alloy LB , & Gibb BE (2012). Number of childhood abuse perpetrators and the occurrence of depressive episodes in adulthood. Child Abuse & Neglect, 36(4), 323–332. 10.1016/j.chiabu.2011.11.007 [PubMed: 22565039]

Maniglio R (2013). Child sexual abuse in the etiology of anxiety disorders: A systematic review of reviews. Trauma, Violence, & Abuse, 14(2), 96–112. 10.1177/1524838012470032

Marshall GN , Miles JNV , & Stewart SH (2010). Anxiety sensitivity and PTSD symptom severity are reciprocally related: Evidence from a longitudinal study of physical trauma survivors. Journal of Abnormal Psychology, 119(1), 143–150. 10.1037/a0018009 [PubMed: 20141251]

Matthews KA , Chang Y-F , Thurston RC , & Bromberger JT (2014). Child abuse is related to inflammation in mid-life women: Role of obesity. Brain, Behavior, and Immunity, 36(0), 29–34. 10.1016/j.bbi.2013.09.013

Miller GE , Chen E , & Parker KJ (2011). Psychological stress in childhood and susceptibility to the chronic diseases of aging: Moving toward a model of behavioral and biological mechanisms. Psychological Bulletin, 137(6), 959–997. 10.1037/a0024768 [PubMed: 21787044]

Muthén LK , & Muthén BO (1998–2015). Mplus user's guide. Los Angeles, CA: Muthén & Muthén.

Nemeroff CB (2016). Paradise lost: The neurobiological and clinical consequences of child abuse and neglect. Neuron, 89(5), 892–909. 10.1016/j.neuron.2016.01.019 [PubMed: 26938439]

Norton PJ , & Asmundson GJG (2003). Amending the fear-avoidance model of chronic pain: What is the role of physiological arousal? Behavior Therapy, 34(1), 17–30. 10.1016/S0005-7894(03)80019-9

Ocañez KLS , Kathryn McHugh R , & Otto MW (2010). A meta-analytic review of the association between anxiety sensitivity and pain. Depression and Anxiety, 27(8), 760–767. 10.1002/da.20681 [PubMed: 20336798]

Patel KV , Guralnik JM , Dansie EJ , & Turk DC (2013). Prevalence and impact of pain among older adults in the United States: Findings from the 2011 National Health and Aging Trends Study. PAIN ®, 154(12), 2649–2657. 10.1016/j.pain.2013.07.029 [PubMed: 24287107]

Pettit JW , Kline J , Gencoz T , Gencoz F , & Joiner T (2001). Are happier people healthier? The specific role of positive affect in predicting self-reported health symptoms. Journal of Research in Personality, 35, 521–536. 10.1006/jrpe.2001.2327

Piazza JR , Charles ST , & Almeida DM (2007). Living with chronic health conditions: Age differences in affective well-being. The Journals of Gerontology: Series B, 62(6), 313–321. 10.1093/geronb/62.6.p313

Pinto R , Correia L , & Maia Â (2014). Assessing the reliability of retrospective reports of adverse childhood experiences among adolescents with documented childhood maltreatment. Journal of Family Violence, 29(4), 431–438. 10.1007/s10896-014-9602-9

Polusny MA , & Follette VM (1995). Long-term correlates of child sexual abuse: Theory and review of the empirical literature. Applied and Preventive Psychology, 4(3), 143–166. 10.1016/S0962-1849(05)80055-1

Preacher KJ , Curran PJ , & Bauer DJ (2006). Computational tools for probing interaction effects in multiple linear regression, multilevel modeling, and latent curve analysis. Journal of Educational and Behavioral Statistics, 31(4), 437–448. 10.3102/10769986031004437

Raphael K , Chandler H , & Ciccone D (2004). Is childhood abuse a risk factor for chronic pain in adulthood? Current Pain and Headache Reports, 8(2), 99–110. 10.1007/s11916-004-0023-y [PubMed: 14980144]

Raphael KG , & Widom CS (2011). Posttraumatic stress disorder moderates the relation between documented childhood victimization and pain 30 years later. Pain, 152(1), 163–169. 10.1016/j.pain.2010.10.014 [PubMed: 21050659]

Resnick HS , Yehuda R , Pitman RK , & Foy DW (1995). Effect of previous trauma on acute plasma cortisol level following rape. American Journal of Psychiatry, 152(11), 1675–1677. 10.1176/ajp.152.11.1675 [PubMed: 7485635]

Romans S , Belaise C , Martin J , Morris E , & Raffi A (2002). Childhood abuse and later medical disorders in women. Psychotherapy and Psychosomatics, 71(3), 141–150. 10.1159/000056281 [PubMed: 12021556]

Rose DT , & Abramson LY (1992). Developmental predictors of depressive cognitive styles: Developmental perspectives on depression In Cicchetti D & Toth SL (Eds.), Developmental perspectives on depression (Vol. 4, pp. 323–349). Rochester Symposium on Developmental Psychopathology.

Rosenbaum PR , & Rubin DB (1983). The central role of the propensity score in observational studies for causal effects. Biometrika, 70(1), 41–55. 10.1093/biomet/70.1.41

Sachs-Ericsson N , Blazer D , Plant EA , & Arnow B (2005). Childhood sexual and physical abuse and the one-year prevalence of medical problems in the National Comorbidity Study. Health Psychology, 24(1), 32–40. 10.1037/0278-6133.24.1.32 [PubMed: 15631560]

Sachs-Ericsson N , Gayman MD , Kendall-Tackett K , Lloyd DA , Medley A , Collins N , … Sawyer K (2010). The long-term impact of childhood abuse on internalizing disorders among older adults: The moderating role of self-esteem. Aging and Mental Health, 14(4), 489–501. 10.1080/13607860903191382 [PubMed: 20455125]

Sachs-Ericsson N , Kendall-Tackett K , & Hernandez A (2007). Childhood abuse, chronic pain and depression in the National Comorbidity Survey. Child Abuse & Neglect, 3(5), 531–547. 10.1016/j.chiabu.2006.12.007

Sachs-Ericsson N , Medley AN , Kendall–Tackett K , & Taylor J (2011). Childhood abuse and current health problems among older adults: The mediating role of self-efficacy. Psychology of Violence, 1(2), 106–120. 10.1037/a0023139 [PubMed: 21922052]

Sachs-Ericsson N , Verona E , Joiner T , & Preacher KJ (2006). Parental verbal abuse and the mediating role of self-criticism in adult internalizing disorders. Journal of Affective Disorders, 93(1–3), 71–78. 10.1016/j.jad.2006.02.014 [PubMed: 16546265]

Sachs-Ericsson NJ , Rushing NC , Stanley IH , & Sheffler J (2016). In my end is my beginning: Developmental trajectories of adverse childhood experiences to late-life suicide. Aging & Mental Health, 20(2), 139–165. 10.1080/13607863.2015.1063107 [PubMed: 26264208]

Sareen J , Henriksen CA , Bolton SL , Afifi TO , Stein MB , & Asmundson GJG (2013). Adverse childhood experiences in relation to mood and anxiety disorders in a population-based sample of active military personnel. Psychological Medicine, 43(1), 73–84. doi:10.1017/s003329171200102x [PubMed: 22608015]

Scarinci IC , McDonald-Haile J , Bradley LA , & Richter JE (1994). Altered pain perception and psychosocial features among women with gastrointestinal disorders and history of abuse: A preliminary model. The American Journal of Medicine, 97(2), 108–118. 10.1016/0002-9343(94)90020-5 [PubMed: 8059776]

Schnittker J , & Bacak V (2014). The increasing predictive validity of self-rated health. PloS One, 9(1), e84933 10.1371/journal.pone.0084933 [PubMed: 24465452]

Scott KM , Von Korff M , Angermeyer MC , Benjet C , Bruffaerts R , de Girolamo G , … Kessler RC (2011). Association of childhood adversities and early-onset mental disorders with adult-onset chronic physical conditions. Archives of General Psychiatry, 68(8), 838–844. 10.1001/archgenpsychiatry.2011.77 [PubMed: 21810647]

Simons LE , Elman I , & Borsook D (2014). Psychological processing in chronic pain: A neural systems approach. Neuroscience & Biobehavioral Reviews, 39, 61–78. 10.1016/j.neubiorev.2013.12.006 [PubMed: 24374383]

Singh T , & Newman AB (2011). Inflammatory markers in population studies of aging. Ageing Research Reviews, 10(3), 319–329. 10.1016/j.arr.2010.11.002 [PubMed: 21145432]

Slavich GM , & Irwin MR (2014). From stress to inflammation and major depressive disorder: A social signal transduction theory of depression. Psychological Bulletin, 140(3), 774–815. 10.1037/a0035302 [PubMed: 24417575]

Smith M , Davis MA , Stano M , & Whedon JM (2013). Aging baby boomers and the rising cost of chronic back pain: Secular trend analysis of longitudinal medical expenditures panel survey data for years 2000 to 2007. Journal of Manipulative and Physiological Therapeutics, 36(1), 2–11. 10.1016/j.jmpt.2012.12.001 [PubMed: 23380209]

Springer KW , Sheridan J , Kuo D , & Carnes M (2007). Long-term physical and mental health consequences of childhood physical abuse: Results from a large population-based sample of men and women. Child Abuse & Neglect, 31(5), 517–530. 10.1016/j.chiabu.2007.01.003 [PubMed: 17532465]

Sullivan PF , Neale MC , & Kendler KS (2000). Genetic epidemiology of major depression: Review and meta-analysis. American Journal of Psychiatry, 157(10), 1552–1562. 10.1176/appi.ajp.157.10.1552 [PubMed: 11007705]

Tanganelli P (2010). Secondary headaches in the elderly. Neurological Sciences, 31(1), 73–76. 10.1007/s10072-010-0277-6

Thompson MP , Kingree JB , & Desai S (2004). Gender differences in long-term health consequences of physical abuse of children: Data from a nationally representative survey. American Journal of Public Health, 94(4), 599–604. 10.2105/ajph.94.4.599 [PubMed: 15054012]

Tietjen G , Karmakar M , Elhai J , & Amialchuk A (2016). Exploring the effect of childhood abuse on migraine, depression and anxiety using structural equation modeling (P2.207). Neurology, 86(16 Supplement).

Tietjen GE , Brandes JL , Peterlin BL , Eloff A , Dafer RM , Stein MR , … Khuder SA (2010). Childhood maltreatment and migraine (Part II). Emotional abuse as a risk factor for headache chronification. Headache: The Journal of Head and Face Pain, 50(1), 32–41. 10.1111/j.1526-4610.2009.01557.x

Tietjen GE , Buse DC , Fanning KM , Serrano D , Reed ML , & Lipton RB (2015). Recalled maltreatment, migraine, and tension-type headache: Results of the AMPP Study. Neurology, 84(2), 132–140. 10.1212/wnl.0000000000001120 [PubMed: 25540306]

Verma V , Sheikh Z , & Ahmed AS (2014). Nociception and role of immune system in pain. Acta Neurologica Belgica, 115(3), 213–220. 10.1007/s13760-014-0411-y [PubMed: 25547878]

Walker AK , Kavelaars A , Heijnen CJ , & Dantzer R (2013). Neuroinflammation and comorbidity of pain and depression. Pharmacological Reviews, 66(1), 80–101. 10.1124/pr.113.008144 [PubMed: 24335193]

Walsh CA , Jamieson E , MacMillan H , & Boyle M (2007). Child abuse and chronic pain in a community survey of women. Journal of Interpersonal Violence, 22(12), 1536–1554. 10.1177/0886260507306484 [PubMed: 17993640]

Weissbecker I , Floyd A , Dedert E , Salmon P , & Sephton S (2006). Childhood trauma and diurnal cortisol disruption in fibromyalgia syndrome. Psychoneuroendocrinology, 31(3), 312–324. 10.1016/j.psyneuen.2005.08.009 [PubMed: 16274933]

Widom CS , Czaja SJ , Bentley T , & Johnson MS (2012). A prospective investigation of physical health outcomes in abused and neglected children: New findings from a 30-year follow-up. American Journal of Public Health, 102(6), 1135–1144. 10.2105/ajph.2011.300636 [PubMed: 22515854]

Widom CS , & Shepard RL (1996). Accuracy of adult recollections of childhood victimization: Part 1. Childhood physical abuse. Psychological Assessment, 8(4), 412–421. 10.1037/1040-3590.8.4.412

Wittchen H (1994). Reliability and validity studies of the WHO–Composite International Diagnostic Interview (CIDI): A critical review. Journal of Psychiatry Research, 28(1), 57–84. 10.1016/0022-3956(94)90036-1

World Health Organization. (1990). Composite International Diagnostic Interview Version 1.0. Geneva, Switzerland: World Health Organization.

Wu S , Wang R , Zhao Y , Ma X , Wu M , Yan X , & He J (2013). The relationship between self-rated health and objective health status: A population-based study. BMC Public Health, 13(1), 1 10.1186/1471-2458-13-320 [PubMed: 23280303]

Yehuda R , Halligan SL , & Bierer LM (2002). Cortisol levels in adult offspring of Holocaust survivors: Relation to PTSD symptom severity in the parent and child. Psychoneuroendocrinology, 27(1–2), 171– 80. 10.1016/s0306-4530(01)00043-9 [PubMed: 11750777]

Yehuda R , Kahana B , Schmeidler J , Southwick SM , Wilson S , & Giller EL (1995). of cumulative lifetime trauma and recent stress on current posttraumatic stress disorder symptoms in holocaust survivors. American Journal of Psychiatry, 152(12), 1815–1818. 10.1176/ajp.152.12.1815 [PubMed: 8526254]

Yeung E , Davis M , & Ciaramitaro M (2015). Cortisol profile mediates the relation between childhood and pain and emotional symptoms among patients with fibromyalgia. Annals of Behavioral Medicine, 1–11. 10.1007/s12160-015-9734-z [PubMed: 24841509]

Zimmerman M , Coryell W , Pfohl B , & Stangl D (1988). The reliability of the fam-history method for psychiatric diagnoses. Archives of General Psychiatry, 45(4), 320–322. 10.1001/archpsyc.1988.01800280030004 [PubMed: 3281625]

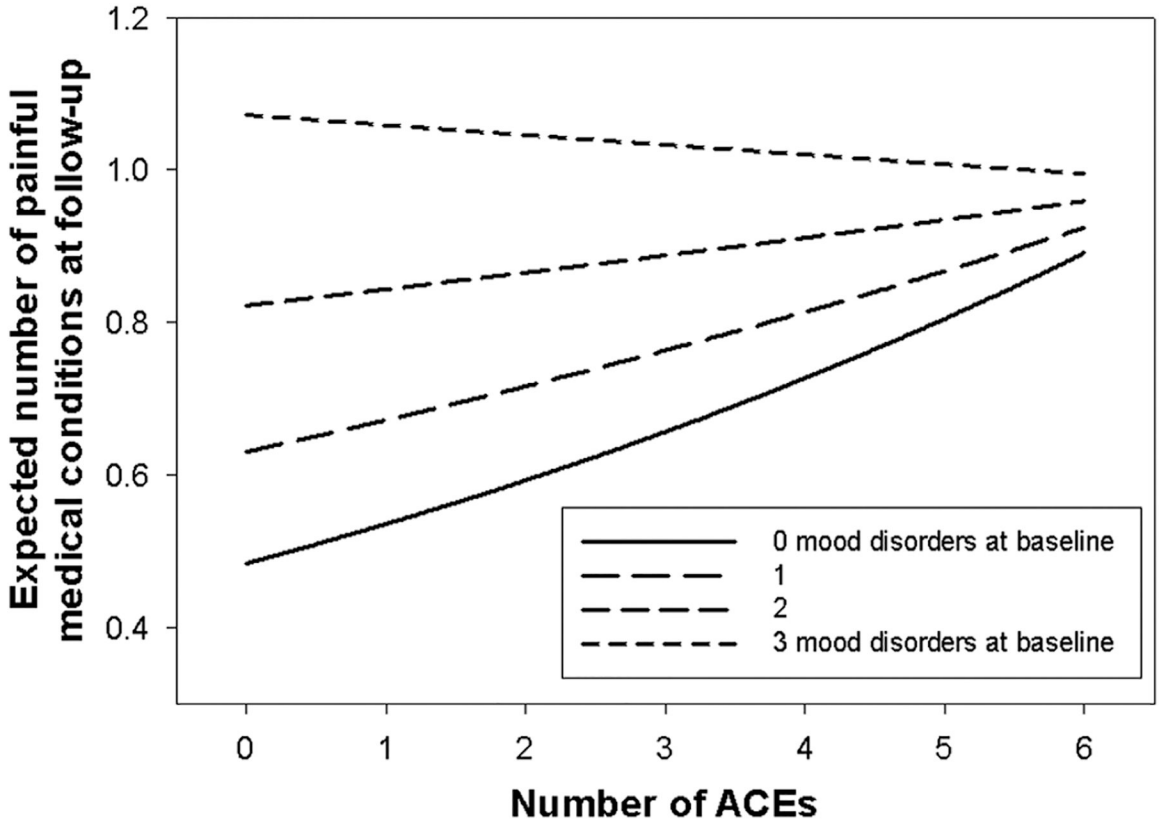

Figure 1.

The interaction of ACEs and anxiety/mood disorders on painful medical conditions.

Note. We show the predicted number of painful medical conditions on the vertical axis, and the simple ACE count on the horizontal axis. The relationship between ACE count and number of painful medical conditions at follow-up is plotted for each number of mood disorders at baseline (0–3). We excluded ACE counts above 6 and mood disorders above 3 due to the very small number of cases with extreme values.

Table 1

Frequency and/or Severity of Individual ACE Categories

Childhood abuse experiences				
Verbal abuse	Never = 51.3%	Rarely = 20.1%	Sometimes = 19.3%	Often = 9.3%
Physical abuse	Never = 95.2%	Rarely = 0.7%	Sometimes = 1.5%	Often = 2.6%
Sexual abuse	Never = 96.0%	Once = 1.0%	More than once = 2.9%	–
Perceived family-of-origin income[a]				
1 = 19.7% (1 = A lot better off)	2 = 69%	3 = 3.3%,	4 = 4.8%	5 = 2.9% (5 = A lot worse off)
Early parental loss				
Lost parent due to divorce, death, or abandonment			No = 78.2%	Yes = 21.8%
Parental psychopathology				
	Mean (*SD*) of Symptoms		Percent with no Symptoms	
Father internalizing	1.8 (3.8)		74.7%	
Mother internalizing	2.9 (4.9)		64.0%	
Father externalizing	1.1 (2.3)		68.7%	
Mother externalizing	0.5 (1.7)		86.7%	

Note. ACE = adverse childhood experiences; SD standard deviation.

[a]Participants were asked to compare their family of origin's financial status during childhood to the average family in their community when growing up, on a scale ranging from 1 (a lot better off) to 5 (*a lot worse off*)

Table 2

Lifetime Psychiatric Diagnoses Assessed at Baseline as a Function of Simple Count of the Number of ACEs[a]

		Psychiatric diagnosis (%)						Pain conditions	
No. ACEs	**% of Population**	**Depression**	**Bioloar**	**GAD**	**Social phobia**	**PD**	**PTSD**	***M***	***SD***
0	41.5	10.5	0.6	2.4	9.1	1.6	2.8	0.66	0.9
1	31.5	16.4	1.3	4.5	12.5	2.4	4.9	0.84	0.99
2	14.5	25.2	2.9	6.4	19	6.5	11.3	0.93	1.1
3	8.0	26.9	2.3	10.0	20.5	6.8	13.8	1.1	1.1
4 to 7	4.4	41.18	7.4	14.9	32.0	9.4	42.3	1.3	1.3

Note. ACEs = adverse childhood experiences; GAD = generalized anxiety disorder; PD = panic disorder; PTSD = posttraumatic stress disorder; M = mean; SD = standard deviation.

[a]For this table, we identified the simple count of each of the ACEs (e.g., present = 1 or absent = 0, the poterntial range was 0 to 9. However, the actual range was 0 to 7).

Table 3

Poisson Regression for Painful Conditions

Variable	*B*	*SE*	Exp (B)	p-value	95% CI
Model 1					
Age	**.018**	**.002**	**1.019**	**<.001**	**[1.016,1.021]**
Sex	**.285**	**.033**	**1.330**	**<.001**	**[1.248,1.418]**
Race (% White)	.055	.038	1.057	.149	[.980, 1.140]
Years of education	**−.053**	**.006**	**.949**	**<.001**	**[.937, .961]**
Model 2					
Verbal abuse	**.092**	**.016**	**1.096**	**<.001**	**[1.062, 1.132]**
Physical abuse	.040	.028	1.041	.157	[.985, 1.100]
Sexual abuse	**.184**	**.039**	**1.202**	**<.001**	**[1.114, 1.296]**
Model 3					
Father internalizing symptoms	**.015**	**.004**	**1.015**	**<.001**	**[1.006, 1.023]**
Mother internalizing symptoms	**.023**	**.003**	**1.023**	**<.001**	**[1.016, 1.030]**
Father externalizing symptoms	**.023**	**.007**	**1.023**	**<.001**	**[1.009, 1.037]**
Mother externalizing symptoms	−.011	.010	.989	.277	[.969, 1.009]
Early parental loss	**.092**	**.038**	**1.096**	**.014**	**[1.019, 1.180]**
Family of origin income	−.009	.019	.991	.636	[.954, 1.029]
Model 4					
Baseline health problems	**.066**	**.021**	**1.069**	**<.001**	**[1.026, 1.113]**
Baseline pain	**.208**	**.022**	**1.232**	**<.001**	**[1.179, 1.287]**
Model 5					
Generalized anxiety disorder	.030	.069	1.030	.664	[.900, 1.179]
Social phobia	.073	.045	1.076	.101	[.986, 1.174]
Panic disorder	.114	.077	1.121	.140	[.963, 1.304]
Posttraumatic stress disorder	**.238**	**.057**	**1.269**	**<.001**	**[1.136, 1.417]**
Major depressive disorder	**.190**	**.043**	**1.209**	**<.001**	**[1.111, 1.316]**
Bipolar I	**.225**	**.099**	**1.252**	**.023**	**[1.031,1.520]**

Note. SE = standard error; CI = confidence interval.