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*

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. J. Clin. Psychol. 73:1403–1428, 2017.

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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

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

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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 at follow-up (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

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*)

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

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).

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).

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.

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

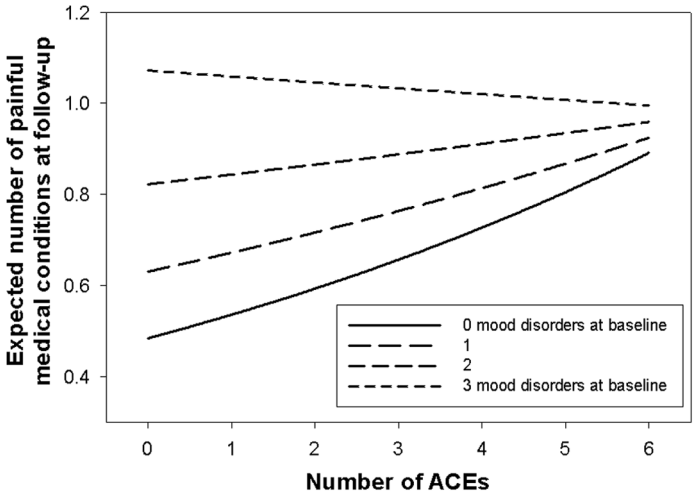

Figure 1. The interaction of ACEs and anxiety/mood disorders on painful medical conditions.
Note. We show the predicted number of painful medical conditions on the vertical axis, and the simple ACE count on the horizontal axis. The relationship between ACE count and number of painful medical conditions 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.

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.

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