Archives of Health Science
Research Article

Adverse Childhood Experiences Association with Health: Perceived Stress and Depression Mediators

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Abstracts

Objective: Adverse Childhood Experiences (ACEs) increase stress reactivity via dysregulation of the hypothalamic-pituitary-adrenal (HPA) axis. This stress reactivity leads to increased inflammation that likely contributes to worse physical and mental health. This investigation examined the relationships between ACEs, mental health, and physical health three to five years later.

Method: Data were obtained from 5,976 adult participants of the Bio psychosocial Religion and Health Study (BRHS) to assess ACEs, perceived stress, and mental and physical health outcomes from 2006 to 201.

Results: Hayes Process Macro was used to model serial mediation between ACEs, perceived stress, depression, and physical health over time. The relationship between ACEs and physical health was partially mediated by perceived stress and depression. These mediators accounted for 44% of the change in physical health over three to five years.

Discussion: ACEs, perceived stress, and depression predicted physical health in mid to late life demonstrating that early adversity and related mental health concerns may ultimately lead to worse health in late life.

Keywords: adverse childhood experiences, physical health, depression, perceived stress,

Introduction

Adverse Childhood Experiences (ACEs) include household dysfunction and child abuse with most adults and children in the U.S. having at least one of these experiences that impacts long term development and health (U.S. Department of Health & Human Services, 2022). Researchers consistently document negative, long-term effects of ACEs exposures and there has been recent discussion of how exposures cluster and predict outcomes differently depending on the type of abuse and dysfunction (Dong et al., 2004). The aggregate impact ACEs is often assessed by a retrospective self-report of adversity including sexual, physical, and/or psychological abuse, neglect, and/or household dysfunction before age 18as documented official child abuse reports are found to be underreported (Felitti et al., 1998). ACEs assessed as a continuous variable, as 2 to 4 factor scores or as ACEs categories (0, 1-3 and 4+) are all associated with physical health conditions such as overweight or obesity, diabetes, heart and respiratory diseases, and cancer (Hughes et al., 2017; Hughes et al., 2021; Petruccelli, Davis, & Berman, 2019). There are recent calls for further studies to examine the potential pathways that link ACEs and health outcomes to encourage psychosocial interventions to improve adult health though few studies have focused on these mechanisms and few studies employ longitudinal designs to fully assess potential mediators (Bourassa et al., 2023; Hales, Saribaz, Debowska, & Rowe, 2022; Soares, Rocha, Kelly-Irving, Stringhini, & Fraga,

2021). Currently, the main hypotheses are that ACEs and health are linked via stress perceptions, increased stressful life event exposures, negative emotion and/or poor health behaviors (Bourassa et al., 2023). Our lab has previously reported links between ACEs and health behaviors leading to negative health outcomes (Morton, Lee, & Spencer-Hwang, 2021; Tan, Morton, Lee, Hartman, & Lee, 2020) and in the present study we will further examine the stress and depressive symptom mediators. One primary hypothesis is that ACEs predict disruptions in stress reactivity or lead to increased stressful life events as mediators leading to poor health (Scorza et al., 2022). What is new in this paper is that we use longitudinal methods to investigate the mediating effects of perceived stress and depressive symptoms.

Theoretically, chronic stress reactivity, either over or under activation, is a potential mechanism linking ACEs to worse health (Berens, Jensen, & Nelson, 2017; Levine, Cole, Weir, & Crimmins, 2015; McEwen & Seeman, 1999; Miller et al., 2009). Neurobiological evidence suggests that chronic, early, life stress dysregulates the hypothalamic-pituitary-adrenal (HPA) axis during brain development (Heim et al., 2002; Ouellet-Morin et al., 2011) viachanges in corticolimbic structures (e.g., hippocampus and amygdala) leading to nonadaptive stress responses (Brietzke et al., 2012; Lim, Radua, & Rubia, 2014), oxidative stress (Kanterman, Sade-Feldman, & Baniyash, 2012) and deficits inappropriate down-regulations of the inflammatory response regardless of the stressor (Cole, 2013; Hostinar, Lachman, Mroczek, Seeman, & Miller, 2015; Irwin & Cole, 2011; Levine et al., 2015; Miller et al., 2009).

Stress perceptions do relate to inflammation and depression (Danese et al., 2011; Heim & Nemeroff, 2001; Kessler, 1997; Niemegeers et al., 2016) above and beyond the effects of other known risk factors (Danese et al., 2008). Inflammation up regulates indoleamine-dioxygenase (Dobos, 2014) that impacts the production and metabolism of serotonin leading to depressive symptoms (Berends, Luiten, & Nyakas, 2005; Dobos, 2014; Miller, Haroon, Raison, & Felger, 2013). ACEs may therefore be linked to physical health via stress perceptions and depressive symptoms resulting from disruptions in the inflammatory system (Kaufman et al., 2004; Miller et al., 2013).

We hypothesize that ACEs are associated with physical health via perceived stress and depressive symptoms as mediators (Moussavi et al., 2007). Overall, we posit that ACEs and physical health are associated indirectly through perceived stress that is mediated by depressive symptoms. We test three models in mid-to-late life: (A) ACEs are positively associated with physical health 3 to 5 years later after controlling for known covariates (age, gender, ethnicity, child and current poverty, time between surveys); (B) the ACEs and physical health relationship is mediated by perceived stress assessed 3 to 5 years earlier; and (C) the ACEs and perceived stress relationshipis then mediated by depressive symptoms also measured 3 to 5 years earlier.

Methods

Participants and Procedures

This study data was from the Bio psychosocial Religion and Health Study (BRHS) (Lee et al., 2009), a sub study of the Adventist Health Study-2 (AHS-2) (Butler et al., 2008). AHS-2 was a cohort study of 97,000 Black and White Seventh-day Adventists (SDA) across North America in 2002-6. Participants who were over 35 years of age and proficient in English were recruited by church pastors in congregations as well as via articles in church magazines and television programs to complete a 50-page questionnaire on lifestyle and health. Of these, a random sample of 21,000 were invited to participate in the BRHS in 2006-7 and 10,869 returned complete surveys. Of these, 6,524 responded again in 2010-11 (3 to 5 years later) to a survey on religion, stress, adverse events, mental and physical health. After omitting cases with more than 10% missing data and those who were of any ethnicity other than Black or White, 5,976 participants were available for multiple imputation for the current project (see Table 1). The 548 who were excluded from analysis due to missing data were older, less educated, more depressed, had worse

physical health, fewer ACEs, and were more likely to be male. There was no difference between included and excluded participants on ethnicity, difficulty meeting expenses for basic needs (for food, clothing, or housing) in the last year and before age 18, or perceived stress.

Measures

Demographic Characteristics

Participants' gender (Female, Male), ethnicity (White, Black), and education (Grade School, Some High School, High School, Trade School, Some College, Associate, Bachelor's, Master's, or Doctoral degree) were based on responses from the AHS-2 baseline questionnaire. Age and difficulty meeting expenses for basic needs (food, clothing, and housing) in the last year and before age 18 (Pudrovska, Schieman, Pearlin, & Nguyen, 2005)were reported in BRHS in 2006-7 on a 5-point Likert scale from (0 = *Not at all*, 4 = *Very*) to assess current and childhood poverty as a control variable.

Adverse Childhood Experiences

ACEs score was a 0-9 count of experiences before the age of 18 including (1) psychological abuse (2 items) (Ryff, Singer, & Palmersheim, 2004), (2) sexual abuse before the age of 13 (1 item) (Cusack, Frueh, & Brady, 2004), (3) physical abuse (4 items) (Ryff et al., 2004); (4) neglect (1 item) (Ryff et al., 2004); (5) living with a substance abuser in childhood (1 item) (Cusack et al., 2004); Felitti, et al., 1998) and (6) separated/divorced parents(Dong et al., 2005),(7) living with a household member who was mentally ill or who attempted suicide when respondent was between ages 8 and 18 (2 items), (8) a household member was incarcerated when respondent was between ages 8 and 18 (1 item), or (9) mother treated violently (5items) (Anda et al., 2006). Questions 1-6 were assessed in the 2006-7 BRHS questionnaire and questions 7-9 in the 2010-11 BRHS questionnaire. For each item endorsed as anything other than never, participants were given a score of one. ACEs scores were then categorized as either no ACEs, low (1-3) ACEs, or high (4-9) ACEs as a cut point for negative consequences after ACEs has been suggested as four or more and this method has been used in previous studies in our lab(Briggs, Amaya-Jackson,

Putnam, & Putnam, 2021; Hamby, Elm, Howell, & Merrick, 2021).

Perceived Stress

The Perceived Stress Scale (PSS) short form (Cohen, Kamarck, & Mermelstein, 1983), a four-item measure of participants' perception of stress in the last month, assessed perceived stress in 2006-7 and was rated on a five-point Likert scale (1 = *Never*; 5 = *Very often*). Higher average scale scores indicate higher perceived stress.

Depressive Symptoms

Depressive symptoms were assessed using the Center for Epidemiological Studies Depression (CES-D) 11-item short form in 2006-7(Gellis, 2010; Kohout, Berkman, Evans, & Cornoni-Huntley, 1993). Scores on the short form scaling were converted with the Kohout algorithm to provide a generalized T score transformation by gender standardized against the NHANES-I(Kohout et al., 1993)and log transformed to address skew.

Physical Health

The Short Form Health Survey was developed for the Medical Outcomes Study, a multi-year study of patients with chronic conditions(Ware, 2000). Originally 36-Items, the SF-12-Item version was developed to reduce response burden(Ware, Kosinski, & Keller, 1998). The SF-12 measures eight domains of functioning and wellbeing: physical functioning, role limitations due to physical problems, bodily pain, general health perceptions, vitality, social functioning, role limitations due to emotional problems, and mental health. Physical health was assessed using the PCS-12. Data was collected in the 2010-11 BRHS questionnaire and scored via a weighted algorithm provided by Ware et al. (1998) assessing general health and how physical health limited the ability to do moderate activities, climb several flights of stairs, accomplish as much as they'd like, and the kinds of work/activities they could engage in, and how much physical pain interfered with daily life. Scores range from 0-100, with higher scores indicating better physical health(Ware et al., 1998). The physical health measure was assessed 3 to 5 years after the psychosocial mediators of perceived stress and depressive symptoms.

Time between Surveys

Because the BRHS 2006-7 and the BRHS 2010-11 survey waves had participants completing the questionnaires between three and five years apart, the time between surveys was controlled.

Analysis

SPSS version 26 was used to analyze the data. Missing data was accounted for with multiple imputation(Graham, 2009), using five samples if fewer than 10% of the variables were missing. The generalized linear model procedure was used with the robust covariance matrix estimator. Testing of mediation was done using PROCESS (Hayes, 2019).

Results

The study sample included 5,976 participants with a mean age of 62 years. Of these, 67% were female, 71% were White, and 58% were college graduates. Forty-eight percent of the participants had no or a little difficulty meeting expenses for basic needs during childhood, and 88% had no to little difficulty meeting expenses for basic needs in the last year. Twenty-nine percent of participants reported no ACEs, 50% endorsed 1-3 ACEs, and 22% endorsed 4-9 ACEs (see Table 1 for demographics by ACEs group).The ACEs groups differed on every variable except physical health with those reporting 4 or more ACEs being worse on each outcome of interest.

Table 1

Demographic Characteristics of Participants by ACEs Level (N = 5976)

Variable	0 ACEs (n=1705)			1-3 ACEs (n=2959)			4-9 ACEs (n=1312)			p
	M	95% CI Low	High	M	95% CI Low	High	M	95% CI Low	High	
Age	64.74	64.12	65.36	62.12	61.68	62.56	58.30	57.67	58.93	.001
Highest Education[a]	6.09	6.00	6.18	5.90	5.83	5.97	5.76	5.66	5.86	.001
Difficulty Meeting Basic Needs[b]										
Under 18	2.38	2.32	2.44	2.68	2.63	2.73	3.24	3.16	3.32	.001
Last Year	1.36	1.32	1.40	1.45	1.42	1.48	1.67	1.61	1.73	.001
Perceived Stress[d]	1.94	1.91	1.97	2.09	2.07	2.10	2.26	2.21	2.30	.001
Depressive Symptoms[c]	6.83	6.50	7.16	8.56	8.27	8.85	11.01	10.49	11.52	.001
Physical Health[e]	48.14	47.66	48.62	47.88	47.51	48.25	47.57	46.98	48.17	.336
	%			%			%			p
Female	65.2	62.9	67.5	65.3	63.6	67.0	72.6	70.2	75.0	.001
White	78.7	76.8	80.6	68.6	66.9	70.3	65.9	63.3	68.5	.001

a1=Grade School, 9=Doctoral Degree

b1 = Not at all to 5= Very

cFull sample M = 8.60, SD = 8.25

d1=Never, 5 = Very often

e Scale score. In national sample M = 50, SD = 10

Adverse Childhood Experiences Association with Health: Perceived Stress and Depression Mediators

A hierarchical multiple regression was conducted to determine whether the addition of ACEs, perceived stress, and depression predicted physical health over and above demographic covariates (see Table 2). In all models, demographic covariates (age, gender, ethnicity, education, current and childhood difficulty meeting expenses for basic needs, and time between surveys) were included in Step 1. ACEs were entered into Model 1 and led to an increase in R^2 of .004, $F(1, 5948) = 27.691$ $p < .001$. Perceived stress was added in Model 2 and led to an increase in R^2 of .008, $F(1, 5947) = 55.067$, $p < .001$. Depressive symptoms was added in Model 3 and led to an increase in R^2 of .008, $F(1, 5946) = 62.521$, $p < .001$. The full model indicates that ACEs, perceived stress, and depression are all negatively associated with physical health, $R^2 = .195$, $F(9, 5946) = 160.519$, $p < .001$, adjusted $R^2 = .194$.

Table 2

Hierarchical Regression Predicting Physical Health

Variable	Model 1			Model 2			Model 3		
	B	t	p	B	t	p	B	t	p
Age	-0.317	-30.055	0.000	-0.327	-30.878	0.000	-0.321	-30.421	0.000
Gender	-2.026	-7.530	0.000	-1.922	-7.166	0.000	-1.579	-5.835	0.000
Ethnicity	0.407	1.446	0.148	0.284	1.012	0.312	0.206	0.737	0.461
Highest Education	0.477	7.120	0.000	0.442	6.605	0.000	0.420	6.311	0.000
Difficulty Meeting Basic Needs									
Under 18	-0.162	-1.722	0.085	-0.130	-1.388	0.165	-0.135	-1.449	0.147
Last Year	-1.169	-8.666	0.000	-0.927	-6.681	0.000	-0.856	-6.174	0.000
Time	-0.001	-1.421	0.155	-0.001	-1.388	0.165	-0.001	-1.288	0.198
ACEs	-0.945	-5.130	0.000	-0.829	-4.505	0.000	-0.666	-3.613	0.000
Perceived Stress				-1.268	-7.167	0.000	-0.556	-2.804	0.005
Depression							-2.228	-7.787	0.000

Serial mediation analysis utilizing Hayes Process Macro (Hayes, 2019) tested whether the association between ACEs and physical health was mediated by perceived stress and depression assessed 3 to 5 years before after controls (see Figure 1). The direct effect of ACEs on physical health was significant, as were the total direct and indirect effects (see Table 3). Perceived stress and depression partially mediated

the relationship between ACEs and physical health, and accounted for 43.9% of the change in physical health (R^2 = 0.439, F(10, 5870) = 139.782, $p < .0001$).

Table 3				
Unstandardized Direct and Indirect Effects of ACEs on Physical Health				
Outcome	B	SE	95% CI	
Direct Effects				
ACEs - Physical Health	-0.651	0.184	-1.012	-0.291
Indirect Effects				
ACEs - Perceived Stress - Physical Health	-0.061	0.038	-0.367	-0.218
ACEs - Depression - Physical Health	-0.163	0.028	-0.220	-0.111
ACEs - Perceived Stress - Depression - Physical Health	-0.066	0.013	-0.093	-0.043
Controlling for Demographic and Time variables				
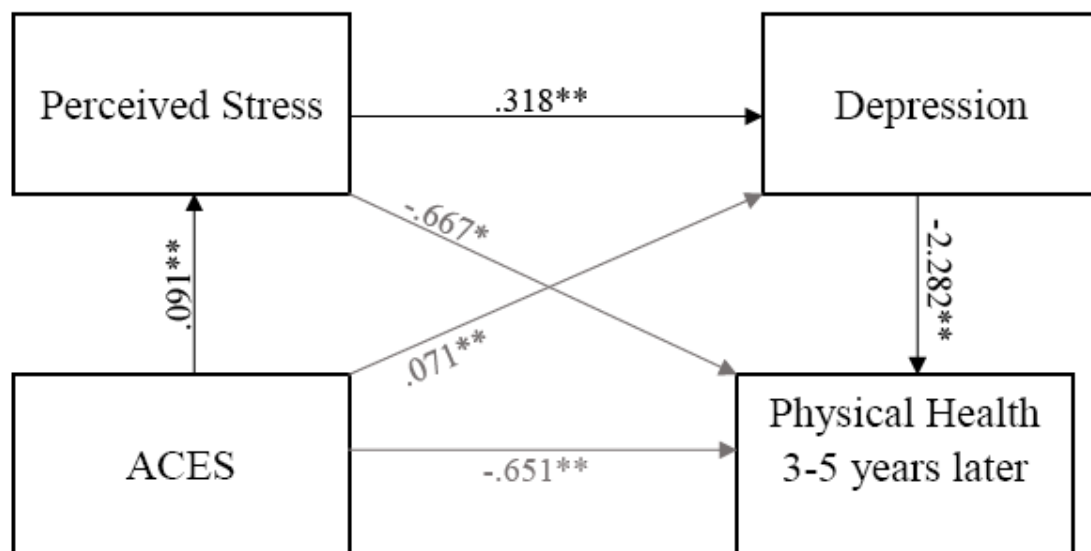
Figure 1. Serial mediation of Perceived Stress and Depression * $p < .05$, ** $p < .000$

Discussion

This study examines the relationship between ACEs and physical health in mid to late life and whether psychosocial mediators assessed 3 to 5 years earlier mediate this relationship. Previous studies indicate that ACEs change the brain structurally in childhood to disrupt and dysregulate the functioning of the HPA axis leading to a less adaptive response to stress (Brietzke et al., 2012; Heim et al., 2002; Lim et al., 2014; Ouellet-Morin et al., 2011). This disruption can either change stress perceptions or increase stress reactivity or lead to increased stressful life events. Any of these stress responses can adversely impact biological mechanisms that disrupt physical health in adulthood. As such, ACEs, perceived stress, and depressive symptoms were examined longitudinally to predict perceived physical health three to five years later after controlling for known covariates. The ACEs

theory (Felitti et al., 1998) proposes that ACEs disrupt physical health via dysregulating stress reactions and mental health to lead to chronic inflammation and poor health outcomes. This aspect of the ACEs theory is supported here as ACEs and perceived stress/depressive symptoms did predict physical health 3 to 5 years later.

After controls, ACEs were associated with physical health has expected and as others have reported (Hales et al., 2022; Hughes et al., 2017; Maschi, Baer, Morrissey, & Moreno, 2013). However, we identify here perceived stress and depression as psychosocial mediators of the ACEs and health relationship. Other studies should examine inflammation in relation to stress perceptions and depressive symptoms to fully understand the pathway identified here. These findings are consistent with other BRHS studies that report ACEs are linked to health via perceived stress and dietary intake patterns

(Tan et al., 2020), via mental health(Morton, Lee, Haviland, & Fraser, 2012), and via mental health and health behaviors (Morton et al., 2021). What is added here is that ACEs may "get under your skin" by disrupting stress responses in the HPA axis that predict health 3 to 5 years later via stress perceptions and depression. The total indirect effect of ACEs on physical health through perceived stress and depressive symptoms accounted for 19.5% of the variance in physical health which is a large effect (Cohen, 1988).

This study addresses gaps in the literature identified by various authors on the impact of childhood trauma on physical health in adulthood. This study has several strengths. First, this study uses a consistent, well defined, and empirically supported definition of childhood trauma as ACEs exposures. Systemic reviews of ACEs literature frequently cite the lack of standardization of ACEs definition and measurement (Hales et al., 2022; Maschi et al., 2013; Mathews, Pacella, Dunne, Simunovic, & Marston, 2020; Soares et al., 2021).In addition, other studies assess for only four or five ACEs (Hughes et al., 2017; Mathews et al., 2020). In this national sample, we assess nine of the ACEs recommended by Dong et al, (2005). Third, this study accounts for poverty in childhood, a factor that likely influences relations between ACEs and health as well as current poverty and level of education to control for environmental risks to focus the examination on psychosocial mediators (Hales et al., 2022; Hughes et al., 2017). Fourth, this study identifies a psychosocial pathway through which ACEs may impact health across the lifespan with a longitudinal design(Hales et al., 2022).This investigation offers a test of the ACEs and health relationship in anationally representative cohort of healthy older adults by including mediators three to five years before the physical health measurement. Finally, study scales were validated and had been used reliably in other ACEs studies. Other research has verified that child abuse self-reports are valid though slightly underreported. Therefore, the strength of these relationships may be stronger than what is reported here.

Several study limitations should also be noted. Study participants were all from the Seventh-day Adventist (SDA) church and were relatively healthy and educated. SDAs typically have healthy dietary intake and lifestyles based on SDA church doctrinal beliefs(Hummer, Ellison, Rogers, Moulton, & Romero, 2004). Therefore, again these associations may be stronger in a general sample of the community. The assessment of perceived stress does not allow us to understand whether the participants had more stressors in their lives or whether they simply reacted to stressors more strongly than other participants.

Future directions for this area of study should continue to examine the mechanisms proposed by Felitti to fully understand the changes in neurodevelopment that disrupt perceived stress, mental health, and subsequent health behaviors that lead to worse health and shorter life spans. The BRHS to date has evidence that poor dietary patterns can follow from disrupted mental health and emotional regulation after ACEs exposures to shorten longevity. Understanding these mechanisms of action further is needed to propose prevention and treatment of ACEs.

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