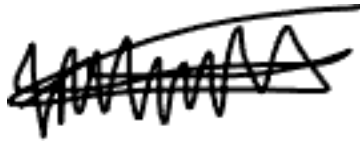


Distribution Agreement

In presenting this thesis as a partial fulfillment of the requirements for a degree from Emory University, I hereby grant to Emory University and its agents the non-exclusive license to archive, make accessible, and display my thesis in whole or in part in all forms of media, now or hereafter now, including display on the World Wide Web. I understand that I may select some access restrictions as part of the online submission of this thesis. I retain all ownership rights to the copyright of the thesis. I also retain the right to use in future works (such as articles or books) all or part of this thesis.

Eugenia Giampetruzzi

A handwritten signature in black ink, appearing to be 'Eugenia Giampetruzzi', written over a horizontal line.

March 13, 2023

Childhood Adversity and Psychiatric Diagnoses: The Role of Protective Factors

by

Eugenia E. Giampetruzzi

Allison M. LoPilato, Ph.D.
Co-Advisor

Elaine F. Walker, Ph.D.
Co-Advisor
Psychology

Allison M. LoPilato, Ph.D.
Co-Advisor

Elaine F. Walker, Ph.D.
Co-Advisor

Rachel Hershenberg, Ph.D.
Committee Member

Patricia Brennan, Ph.D.
Committee Member

2023

Childhood Adversity and Psychiatric Diagnoses: The Role of Protective Factors

By

Eugenia E. Giampetruzzi

Allison M. LoPilato, Ph.D.

Co-Advisor

Elaine F. Walker, Ph.D.

Co-Advisor

An abstract of
a thesis submitted to the Faculty of Emory College of Arts and Sciences
of Emory University in partial fulfillment
of the requirements of the degree of
Bachelor of Arts with Honors

Psychology

2023

Abstract

Childhood Adversity and Psychiatric Diagnoses: The Role of Protective Factors By Eugenia E. Giampetruzzi

Introduction: An abundance of research has established that adverse childhood experiences (ACEs) confer risk for psychiatric diagnoses, and that protective factors may moderate this association. Research exploring the effect of different types of protective factors in the relationship between ACEs and internalizing disorders (e.g., depression, anxiety) is more limited. The purpose of the present study was to 1.) investigate the relationship between ACEs and risk for diagnosis of a depressive, or anxiety disorder, suicidality, and substance use difficulties, 2.) examine whether protective factors moderate this relationship, and 3.) determine whether internal personal facets and external environmental facets differentially impact these associations.

Methods: 688 participants aged 12-30 ($M = 18.17$; $SD = 4.05$) identified as youth at clinical high risk (CHR) for serious mental illness were assessed using a child adversity interview, protective factors assessment (SAVRY), and diagnostic assessment (SCID-5). Logistic regression analyses were performed to determine whether ACEs predicted a lifetime or current diagnosis of a depressive, or anxiety disorder, history of self-harm or suicide attempts, and substance use difficulties. Moderation regression analyses were then conducted to assess whether these associations were weaker in the presence of protective factors.

Results & Conclusions: Higher levels of cumulative ACEs predicted diagnosis of a current depressive disorder ($\beta = .12(1.13)$, $p = .04$), history of self-harm or suicide attempts ($\beta = .34(1.40)$, $p < .001$), and substance use difficulties ($\beta = .14(1.15)$, $p = .04$). Childhood sexual abuse ($\beta = .77(2.15)$, $p = .001$), emotional neglect ($\beta = .38(1.46)$, $p = .05$), and psychological abuse ($\beta = .42(1.52)$, $p = .04$), specifically predicted a history of self-harm or suicide attempts. Sexual abuse ($\beta = .58(1.79)$, $p = .02$), and emotional neglect ($\beta = .52(1.69)$, $p = .006$), were also associated with diagnosis of a current depressive disorder. Only witnessing violence in the home during childhood uniquely predicted lifetime substance use difficulties ($\beta = .70(2.01)$, $p = .002$). There was no association between ACEs and diagnosis of anxiety disorder, across adversity subtypes, and no moderation effect of protective factors in the relationship between ACEs and psychiatric outcomes. These findings add nuance to a growing literature linking adverse childhood experiences to subsequent psychopathology, and highlights the importance of continued investigation into the mechanisms that may buffer this relationship.

Childhood Adversity and Psychiatric Diagnoses: The Role of Protective Factors

By

Eugenia E. Giampetruzzi

Allison M. LoPilato, Ph.D.

Co-Advisor

Elaine F. Walker, Ph.D.

Co-Advisor

A thesis submitted to the Faculty of Emory College of Arts and Sciences
of Emory University in partial fulfillment
of the requirements of the degree of
Bachelor of Arts with Honors

Psychology

2023

Acknowledgements

I would like to thank my advisor, Dr. Allison LoPilato, for her invaluable guidance on this project, and her expert oversight of my broader research into adverse childhood experiences. In addition to thanking all members of my committee for their valued direction throughout my undergraduate career, I'd like to specifically thank Dr. Rachel Hershenberg and Amanda C. Tan, for their life-changing mentorship and encouragement, as well as Dr. Brandon Kitay, and Dr. Patricio Riva-Posse from the Fuqua Center for Late-Life Depression. Lastly, words cannot express my gratitude for my parents, grandparents, and sister for providing me the opportunity to undertake academic research.

Table of Contents

Introduction.....	1
Methods.....	6
Results.....	9
Discussion.....	12
Table 1. ACEs and Protective Factors.....	17
Table 2. Sample Characteristics.....	18
Table 3. Associations Between ACEs and Clinical Outcomes.....	20
References.....	22

Introduction

It is well-established that adverse childhood experiences (ACE's) increase the risk for psychiatric illness (Kim et al., 2019). Common ACEs include psychological bullying, physical bullying, emotional neglect, psychological abuse, physical abuse, sexual abuse and witnessing violence in the childhood home. Half of all children in the United States report ACEs and those with high levels of adversity are four times more likely to develop a mental disorder than children with no history of adversity. (Green et al., 2010; McLaughlin et al., 2012; McLaughlin et al., 2013; McLaughlin 2017). However, there are a significant proportion of individuals who do not develop mental illness following ACE exposure which drives interest into the factors that support these resilient responses. Growing empirical evidence has found that protective factors, such as strong social support networks and resilient personality traits broadly buffer this long-term risk of mental illness linked to childhood adversity. Both individual and environmental level factors are thought to reduce this risk by strengthening and supporting adjustment and coping mechanisms (Crouch et al., 2019; Cheong et al., 2017). However, it is not yet clear whether protective factors mitigate associations with specific psychiatric outcomes, and whether specific types of protective factors are more potent. Research examining the nuances that determine vulnerability to poor mental health outcomes following ACE exposure can help guide preventative intervention strategies.

ACE's and Psychiatric Diagnoses. A robust literature has shown the long-term mental health and behavioral consequences associated with ACEs (Racine et al., 2020; McCutchen et al., 2022). While most studies have examined the impact of ACEs on mental illness and pathophysiological mechanisms broadly, those that have looked at

specific diagnostic outcomes have tended to focus on substance use and neurodevelopmental disorders. History of ACEs has been found to increase risk for substance use disorders, schizophrenia, attention-deficit-hyperactivity-disorder (ADHD), and autism spectrum disorder (ASD) (Zhang et al., 2022; Wüstner et al., 2019; Cawthorpe et al., 2018; Hughes et al., 2016; Popvic et al., 2019). Interestingly, less research has directly explored the relationship between ACE's and internalizing disorders despite depression and anxiety disorders being the most common psychiatric disorders, and a growing literature on the impact ACE's have on the developmental mechanisms underlying these disorders (e.g., executive functioning (Sheridan et al., 2017) ; emotion processing (Lambert et al., 2016); reward processing (Dennison et al., 2017); physiological reactivity (Busso et al., 2017) ; stress perception (LoPilato et al., 2019). Depression and anxiety are highly comorbid with each other and tend to co-occur with transdiagnostic clinical features such as suicidal ideation and substance use. Even fewer studies examine the buffering effect of protective factors in the relationship between ACEs and internalizing disorders (Kalin, 2020).

Protective Factors. While research tends to focus on risk factors for mental illness, there is growing interest in investigating protective factors. Protective factors are defined as resources that facilitate adaption to childhood adversity (Windle, 2010). These factors can exist at the individual level (e.g., high self-esteem, agreeableness, emotional stability etc.,) and at the environmental level as both family structures (e.g., supportive caregivers) and community involvements (e.g., religious, or spiritual groups; Cicchetti & Toth, 2016). Recent research has examined whether protective factors mitigate the negative effects of ACE exposure (Racine et al., 2020; Reich et al., 2010; Powell et al. 2020; Meng et al.,

2018; Hamby et al., 2018). Racine and colleagues (2020) found that there was a positive association between ACEs and trauma-related distress in individuals who had low levels of protective factors, but not for those with high levels of protective factors. Multiple theories have been forwarded to explain the mechanisms by which protective factors reshape the negative trajectories known to follow ACEs. These mechanisms include: promoting successful functioning across social contexts via nurturing relationships, creating safe and stable environments necessary for proper brain development, supporting development of adaptive emotion regulation skills, increasing access to mental health resources, and reducing behavioral and emotional dysregulation (Howell et al., 2014; Centers for Disease Control and Prevention, 2021).

Different types of protective factors have been linked to positive adaptation despite childhood adversity. For example, higher scores on resilient personality scales have been associated with better mental health outcomes in adults with a history of ACEs (Schnarrs et al., 2020; Chandler et al., 2015). Common items on these resiliency scales include “It does not take me long to recover from a stressful event,” and “I tend to bounce back quickly after hard times” (Smith et al., 2018). Having a strong commitment and/or connection to school has been shown to significantly reduce the odds of co-occurring mental health and substance abuse problems (Lensch et al., 2021). Strong perceived social support, attachment, and bonds have also been shown to moderate the relationship between ACEs and later-life depressive symptoms (Von Cheong et al., 2017). Investigation into the protective factors of positive attitude toward intervention/authority and prosocial involvement is still lacking.

Protective factors encompass a broad range of different experiences, and it is not clear whether internal facets (e.g., personality traits) and external environmental facets (e.g., family and community connections) have different effects. Internal protective factors operate at the level of individual abilities and capacities such as temperament or motivation that can promote adaptation towards positive lifestyle and career outcomes, while external protective factors have been shown to increase access to specialized mental health services (Jean-Thorn et al., 2022). There is limited work comparing how internal vs. external protective factors mitigate risk for mental illness following ACE exposure (Cesar Dias & Cadime, 2017; Vanderbilt-Adriance et al., 2008). A clearer understanding of which types of protective factors mitigate risk is critical to developing more targeted preventative interventions. Bolstering connections and bonds in school may be more beneficial if external facets are more potent, while building resilient personality traits may be a more helpful target if internal facets show stronger protective effects.

The present study.

The purpose of the current study is to 1.) investigate the association between ACE's and diagnosis of depressive disorders, anxiety disorders, history of suicidality, and substance use difficulties 2.) determine whether protective factors moderate these associations and 3.) clarify whether internal personal facets (e.g., resilient personality traits, positive attitude toward intervention/authority, prosocial involvement, and strong commitment to school) and external environmental factors (e.g., strong social support and strong attachment and bonds) differentially impact these associations in a large sample of youth at clinical high risk (CHR) for serious mental illness.

The clinical-high risk population is ideally suited to test the effects of childhood adversity as these samples are enriched for childhood adversity experiences and allow for a wider variation of adversity than what is typically afforded by community samples (Larsson, et al. 2013; Matheson, et al. 2013; Ruby et al. 2014). Childhood adversity and trauma are also associated with psychotic-like experiences, such as low-grade delusion ideation, isolated auditory hallucinations, and perceptual aberrations even among individuals who do not have a psychotic disorder (Janssen et al. 2004; Kelleher et al. 2008). Additionally, CHR samples also provide an enriched range of psychiatric syndromes. In addition to putative prodromal symptoms (i.e., sub threshold positive symptoms), 80% of CHR individuals have comorbid diagnoses of mood, personality, and externalizing disorders that are independent of psychosis outcome (Addington et al., in press).

Based on substantial existing literature linking ACEs to depressive and anxious symptoms, we predict ACEs will be associated depressive and anxiety diagnoses, as well as history of history of self-harm or suicide attempts, and substance use difficulties. We predict that this relationship will be moderated by protective factors, such that the relationship will be stronger in individuals with lower protective factors. We will also explore whether external environmental and internal individual protective factors differentially moderate this relationship.

Methods

Participants

Participants included 688 participants identified as youth at clinical high risk (CHR) for serious mental illness aged 12-30 years ($M=18.17$; $SD= 4.05$) from the North American Prodrome Longitudinal Study (NAPLS-3). Specific details about ascertainment, inclusion, and exclusion criteria have been described at length elsewhere (Addington et al. 2022). All participants were recruited over the course of three years from one of nine NAPLS sites located at Emory University, Harvard University, University of Calgary, University of North Carolina Chapel Hill (UNC), Yale University, Zucker Hillside Hospital, and the University of California at Los Angeles (UCLA), at San Diego (UCSD), and at San Francisco (UCSF) (Addington et al., 2022).

Procedure

Participants in the NAPLS-3 study received an in-depth baseline assessment, and continued monitoring assessments at two, four, six, eight, twelve, eighteen, and twenty-four months. Participants were included in the current study if they completed the child adversity interview, protective factors assessment, and diagnostic assessment at the baseline visit.

Measures

Documentation of Trauma (Pre-Age 18). Documentation of childhood trauma was completed by a study interviewer during the baseline visit for each participant. Types of trauma screened for included: 1) psychological bullying, 2) physical bullying, 3) emotional neglect, 4) psychological abuse, 5) physical abuse, and 6) sexual abuse. Patients responded “yes” or “no” to whether they had experienced each of these subtypes

of trauma prior to the age of 18 yielding dichotomous scores of 0 = has not occurred, or 1 = participant acknowledges, or there is information from reliable sources, that this has occurred. Number of ACEs a patient endorsed were then added together to create a cumulative risk score of the total number of ACE categories (e.g., history of sexual abuse & physical abuse; risk score = 2). Psychological and physical bullying were excluded from the ACE scores and all analyses due to multicollinearity between those subtypes and psychological and physical abuse, respectively.

Structured Clinical Interview for DSM-5 (SCID-5). The SCID-5 was used to systematically assess whether participants met diagnostic criteria for psychiatric diagnoses as outlined in the 5th Edition of the Diagnostic and Statistical Manual of Mental Disorders. Relevant diagnoses for the present study included the following categories: 1) depressive disorders (e.g., Major Depressive Disorder, Persistent Depressive Disorder), and 2) anxiety disorders (e.g., Social Phobia, Generalized Anxiety Disorder). Bipolar (BPAD), Obsessive Compulsive (OCD), Panic, Agoraphobia, Specific Phobia, and Post-traumatic stress (PTSD) disorders were excluded from these categories. The SCID is well correlated with systematic diagnostic interviews in natural clinical settings (Drill et al., 2015; Osorio et al., 2019). Participants were assessed for both lifetime and current disorders.

Structured Assessment of Violence Risk in Youth (SAVRY). Protective factors were recorded using the SAVRY, a semi-structured interview composed of items assessing 24 risk factors and 6 protective factors related to aggression and violence in youth. Protective factors surveyed included 1) prosocial involvement, 2) strong social support, 3) strong attachment and bonds, 4) positive attitude toward

intervention/authority, 5) strong commitment to school, and 6) resilient personality traits. Each factor was marked as either “present” or “absent” for each participant. The risk factors of history of self-harm or suicide attempts, and substance use difficulties, as well as the ACE subtype of exposure to violence in the home were recorded on a range of 1) low versus 2) moderate or high. The predictive validity of the SAVRY is well established across numerous studies with large AUC coefficients ranging from .74 to .80 (Borum et al., 2020).

Data Analysis Plan

All analyses were conducted using SPSS. Logistic regression analyses were performed to model the associations between cumulative ACE risk scores and lifetime and current diagnosis of a depressive, or anxiety disorder (dichotomous yes/no variables), as well as the relationship between cumulative ACE risk scores and history of self-harm or suicide attempts, and lifetime substance use difficulties. To then test the hypothesis that the association between cumulative ACE risk scores and diagnosis of a depressive, or anxiety disorder is weaker in the presence of protective factors, moderation regression analyses were conducted. Both unstandardized and standardized betas are presented; standardized betas appear in parentheses. A significance level of $\alpha < 0.05$ was chosen for all analyses.

Results

Descriptive Statistics.

Sample characteristics. Demographic and clinical characteristics of the sample are shown in Table 2. Participants had an average age of 18.17 years ($SD = 4.05$). Nearly half of the participants were female (45.5%), and 30.8% were non-white. Rates of internalizing disorders were high; 54.1% of the sample met criteria for a current anxiety disorder, 48.1% met criteria for a current depressive disorder, and 41.7% met criteria for a lifetime depressive disorder. Around one-fourth of participants met criteria for a lifetime anxiety disorder (27.4%). 36.5% of participants endorsed a history of self-harm or suicide attempts and 23.9% endorsed substance-use difficulties. Consistent with prior literature, male participants were more likely to report physical abuse ($F(1,686) = 6.43, p = .01$), than female participants. Female participants were more likely than male participants to report emotional neglect ($F(1,686) = 7.35, p = .01$), sexual abuse ($F(1,686) = 13.51, p < .001$), a current depressive disorder ($F(1,685) = 5.86, p = .02$), a current anxiety disorder ($F(1,685) = 9.51, p = .002$), and history of self-harm or suicide attempts ($F(1,672) = 22.48, p < .001$). No sex differences were found for scores of cumulative adversity, the ACE subtypes of psychological abuse and exposure to violence in the home, and lifetime diagnoses or substance use difficulties.

Prevalence of childhood adversity and protective factors. Rates of ACE exposure were high; 60.1% of the sample reported at least one ACE and 35.8% participants reported two or more lifetime ACEs. The two most common subtypes of childhood adversity were emotional neglect (34.9%), physical abuse (29.1%), and psychological abuse (28.6%), followed by violence in the home (21.2%), and sexual

abuse (13.1%; See Table 2). The prevalence of protective factors was low; nearly three-fourths of the sample endorsed no protective factors (70.6%; See Table 2).

Logistic Regression Analyses.

Cumulative ACE risk scores predicted diagnosis of a current depressive disorder ($\beta = .12(1.13)$, $p = .04$), history of self-harm or suicide attempts ($\beta = .34(1.40)$, $p < .001$), and lifetime substance use difficulties ($\beta = .14(1.15)$, $p = .04$). Cumulative ACE risk scores did not predict lifetime diagnosis of a depressive disorder, or lifetime or current diagnosis of an anxiety disorder.

Given concerns about the cumulative risk approach in the literature and its tendency to obscure specific associations (Schafer et al. 2022; Sosnowski et al. 2022; Smith & Pollack, 2020; Evans et al. 2013; McLaughlin et al. 2020), exploratory logistic regression analyses were performed to model the associations between each of the five ACE subtypes (e.g., emotional neglect, physical abuse, psychological abuse, sexual abuse, and violence in the home), and each of the psychiatric outcome variables. Given the high rates of co-occurrence among ACE subtypes (Broekhof et al., 2022; Brown et al., 2018), we controlled for the other ACE subtypes in each model to identify specific associations.

Childhood sexual abuse predicted diagnosis of a current depressive disorder ($\beta = .58(1.79)$, $p = .02$), lifetime depressive disorder ($\beta = .51(1.66)$, $p = .03$), and history of self-harm or suicide attempts ($\beta = .77(2.15)$, $p = .001$). Childhood emotional neglect predicted diagnosis of a current depressive disorder ($\beta = .52(1.69)$, $p = .006$), and history of self-harm or suicide attempts ($\beta = .38(1.46)$, $p = .05$). The related subtype of childhood psychological abuse also predicted history of self-harm or suicide attempts ($\beta =$

.42(1.52), $p=.04$). Only violence in the childhood home predicted lifetime substance use difficulties ($\beta = .70(2.01)$, $p=.002$). No ACE subtype predicted lifetime or current diagnosis of an anxiety disorder.

Moderation Regression Analyses.

Protective factors did not moderate the association between cumulative ACE risk scores and diagnosis of a depressive, or anxiety disorder, history of self-harm and suicide, and substance use difficulties. Exploratory moderation regression analyses were conducted to examine whether protective factors moderated the associations between individual ACE subtypes and diagnosis of a depressive, or anxiety disorder, history of self-harm and suicide, and substance use difficulties. There was no significant moderation in any of the models. This lack of moderation was true for protective factors generally, as well as when grouped by internal versus external protective factors.

Discussion

The present study sought to investigate the association between ACE's and psychiatric outcomes with a focus on the role of protective factors in buffering risk conferred by adverse childhood experiences. By utilizing a large, clinical high-risk youth population we sought to enhance the generalizability of such findings. This research is both timely and necessary as a series of new intervention initiatives attempt to address the global public health threat posed by childhood adversity.

In partial support of our hypothesis, higher levels of childhood adversity were associated with some lifetime negative psychiatric outcomes. Specifically, higher levels of ACEs were associated with diagnosis of a current depressive disorder, history of self-harm or suicide attempts, and substance use difficulties. These results support prior work showing the increased negative risk conferred by multiple ACEs and the relevance of the additive effects of co-occurring ACEs (Henry et al. 2021; Wiens et al., 2020; Suliman et al., 2009; Schilling et al., 2008).

When ACE subtypes were examined separately there was a unique pattern of associations. Consistent with extensive prior literature identifying childhood sexual abuse as a risk factor for clinical depression and long-term suicidality, childhood sexual abuse specifically predicted diagnosis of a current depressive disorder, lifetime depressive disorder, and history of self-harm or suicide attempts, despite being the least common ACE reported in this sample (Gardner et al., 2019; Rapsey, 2019). Childhood emotional neglect and childhood psychological abuse predicted history of self-harm or suicide attempts. Childhood emotional was also associated with diagnosis of a current depressive disorder. These findings contribute to a recent, but growing interest in

investigating the causes and impacts of non-physical subtypes of trauma (CMF Gama et al., 2021). Relative to sexual and physical abuse, the ACE subtype of emotional neglect has been historically understudied in the ACE literature. However, more recent studies suggest emotional maltreatment may yield a greater number of negative life outcomes and lower quality of life ratings than the subtypes of sexual and physical abuse (Strathearn et al., 2020). The specific associations observed in our study may be driven by the underlying psychological impacts of emotional dysregulation and interpersonal problems that have been demonstrated to follow non-physical forms of abuse, and are closely correlated to depressive disorders (Christ et al., 2019).

Interestingly, only the subtype of witnessing violence in the home during childhood uniquely predicted lifetime substance use difficulties. In prior work, the association between childhood adversity and later substance use difficulties has been most frequently associated with sexual and physical abuse (Simpson & Miller, 2002; Walsh et al., 2003). While it's possible that witnessing violence directly increases risk for substance use, it's also possible that violence in the home is a proxy variable for other risk factors such as parental substance abuse or genetic predisposition to addiction. For example, a multitude of studies have revealed that parental substance abuse heightens the risk of childhood exposure to neglect, and domestic violence, as well as long-term negative outcomes such as emotional and behavioral difficulties, and later-life substance misuse (Velleman et al., 2018; Bromfield et al., 2010). Still, these results alone are especially valuable given the unprecedented, simultaneous rise in rates of substance use and domestic violence following the COVID-19 pandemic (Abramson, 2021; Mineo, 2022).

Contrary to our hypothesis, higher levels of ACEs were not associated with current or lifetime diagnosis of an anxiety disorder. These results are in line with recent, yet underdeveloped, longitudinal research that identifies stronger associations of childhood adversity with depressive symptomatology relative to anxious symptomatology (Kuzminskaite et al., 2022). Our findings expand this evolving literature by showing that the distinction between depressive and anxiety disorders in the context of childhood adversity may exist across not only symptomatology and course, but also lifetime and current diagnoses. This can inform research into the developmental mechanisms that may explain the relationship between ACEs and internalizing disorders. For example, these findings may support literature linking childhood adversity to mechanisms implicated in the pathophysiology of depression, such as inhibited behavioral and neural indices of effort-based decision making, and reward processing (Armbruster-Genç et al., 2022; Oltean et al., 2022).

Additionally, our study shows that this lack of association between ACEs and diagnosis of an anxiety disorder is consistent regardless of adversity type. This contradicts evidence uniquely linking childhood sexual abuse to generalized and social anxiety disorders (Cougle et al., 2010). This may stem from the common methodological limitation of examining the effect of an individual subtype (e.g., sexual abuse) without controlling for the effect of others (eg., emotional neglect, psychological abuse; McLaughlin et al. 2020). A strength of the present study is that it avoids obscuring the effect of type of adversity, without overestimating the relationship between one ACE subtype and psychopathology outcomes by entering all ACE subtypes into statistical models simultaneously. Nonetheless, it is noteworthy that ACEs did predict history of

suicidality and substance use since these specific clinical features are indicative of greater acuity and functions impairment in patients that meet criteria for an anxiety disorder.

We additionally did not find any moderation effect of protective factors in the relationship between ACEs and psychiatric outcomes. This may indicate that the impact of ACEs is robust even in the presence of protective factors. However, the strikingly low levels of protective factors (i.e., only 26.3% endorsed any protective factor) in this high-risk youth sample presents both a methodological and practical concern. The restricted range of protective factors in our sample likely limited our ability to detect moderation. However, it may also be that the low rates of protective factors in clinical high-risk populations may be one of the underlying reasons for their clinical status, which is characterized by subthreshold psychotic symptoms and co-morbid psychopathology (i.e., 80%). This underscores the importance of increasing access to protective factors in preventative interventions. While childhood adversity can be difficult to prevent and occur at high rates, interventions that bolster protective factors can help mitigate psychiatric sequelae.

There are several limitations that are worth noting. ACEs were assessed via retrospective self-report and did not include information about timing, duration, or perceived impact, which have been shown to inform chronicity and severity of later-life mental illness (Russotti et al., 2021). The known ACE subtypes of physical neglect and poverty were not captured by our childhood trauma measure, but have been previously linked to internalizing psychiatric disorders (Capistrano et al., 2016; Nikulina et al., 2011). Additionally, the low rates of protective factors may have limited our ability to assess the

moderation effect of protective factors in the relationship between ACEs and psychiatric outcomes.

Taken together, these findings support the substantial evidence showing that ACEs have pervasive negative impacts on both short-term development and long-term life outcomes. Our study strengthens and adds to existing findings that experiencing adverse childhood experiences increases risk for subsequent psychopathology, by specifically focusing on internalizing disorders. This supports directions for future research into the specific mechanisms that link and moderate the relationship between ACEs and psychiatric outcomes.

Tables

Table 1.

ACEs and Protective Factors.

	Operational Definition	Items
Adverse Childhood Experience (ACE)	"... childhood events, varying in severity and often chronic, occurring in a child's family or social environment that cause harm or distress, thereby disrupting the child's physical or psychological health and development (Kalmakis & Chandler, 2013)."	Childhood Emotional Neglect Childhood Physical Abuse Childhood Psychological Abuse Childhood Sexual Abuse Witnessing Violence in the Home
Protective Factor	"Assets and resources within the individual, their life, and environment that facilitate the capacity for adaptation and 'bouncing back' in the face of adversity (Windle, 2011)."	Prosocial Involvement Strong Social Support Strong Attachment and Bonds Positive Attitude toward Intervention/Authority Strong Commitment to School Resilient Personality Traits

Table 2.

Sample Characteristics.

Sample Characteristic	Total (n=688)	Males (n=375)	Females (n=313)
<i>Age, years (mean ± SD)</i>	18.17 ± 4.05	18.43 ± 3.99	17.84 ± 4.11
<i>Race, n (%)</i>			
First Nations	14 (2.0%)	13 (3.5%)	1 (0.3%)
East Asian	42 (6.1%)	23 (6.1%)	19 (6.1%)
Southeast Asian	10 (1.5%)	5 (1.3%)	5 (1.6%)
South Asian	20 (2.9%)	13 (3.5%)	7 (2.2%)
Black	78 (11.3%)	44 (11.7%)	34 (10.9%)
Central/South American	41 (6.0%)	21 (5.6%)	20 (6.4%)
Middle Eastern	7 (1.0%)	6 (1.6%)	1 (0.3%)
White	382 (55.5%)	201 (53.6%)	181 (57.8%)
Native Hawaiian or Pacific islander	2 (0.3%)	N/A	2 (0.6%)
Interracial	91 (13.2%)	48 (12.8%)	43 (13.7%)
<i>ACE Subtype Prevalence</i>			
Emotional neglect	240 (34.9%)	114 (30.4%)	126 (40.3%)
Physical Abuse	200 (29.1%)	124 (33.1%)	76 (24.3%)
Psychological abuse	197 (28.6%)	101 (26.9%)	96 (30.7%)
Violence in the home	143 (21.2%)	76 (20.3%)	67 (21.4%)
Sexual abuse	90 (13.1%)	33 (8.8%)	57 (18.2%)
<i>ACE Amount Prevalence</i>			
0 ACE	259 (37.5%)	144 (38.4%)	115 (36.7%)
1 ACE	168 (24.3%)	104 (27.7%)	64 (20.4%)
2 ACEs	105 (15.2%)	51 (13.6%)	54 (17.3%)
3 ACEs	95 (13.8%)	40 (10.7%)	55 (17.6%)
≥ 4 ACEs	47 (6.8%)	28 (7.5%)	19 (6.1%)
<i>Protective Factors Prevalence</i>			
Prosocial involvement	66 (9.6%)	39 (10.4%)	27 (8.6%)
Strong social support	70 (10.1%)	40 (10.7%)	32 (10.2%)
Strong attachment and bonds	72 (10.4%)	40 (10.7%)	30 (9.6%)
Positive attitude toward intervention/authority	59 (8.6%)	31 (8.3%)	28 (8.9%)
Strong commitment to school	74 (10.7%)	48 (12.8%)	26 (8.3%)
Resilient personality traits	80 (11.6%)	42 (11.2%)	38 (12.1%)
<i>Protective Factors Amount Prevalence</i>			
0 Protective factors	487 (70.6%)	261 (69.6%)	226 (72.2%)
1 Protective factor	60 (10.0%)	41 (10.9%)	28 (8.9%)
≥ 2 Protective factors	112 (16.3%)	62 (16.5%)	50 (16.0%)
<i>Psychiatric Disorders Prevalence</i>			
Current anxiety disorder	373 (54.1%)	151 (40.3%)	163 (52.1%)
Lifetime anxiety disorder	189 (27.4%)	105 (28.0%)	83 (26.5%)
Current depressive disorder	332 (48.1%)	165 (44.0%)	167 (53.4%)

Lifetime depressive disorder	288 (41.7%)	146 (38.9%)	142 (45.4%)
History of self-harm or suicide attempts	252 (36.5%)	108 (28.8%)	144 (46.0%)
Lifetime substance-use difficulties	165 (23.9%)	90 (24.0%)	75 (24.0%)

*Percentages may add up to > 100% because one subject can score multiple items or < 100% due to missing data.

Table 3.

Associations Between ACEs and Clinical Outcomes.

ACE	Anxiety				Depression				Clinical Features			
	Current		Lifetime		Current		Lifetime		Self-Harm/Suicide		Substance Use Difficulties	
	β	SE	β	SE	β	SE	β	SE	β	SE	β	SE
Cumulative												
ACE Total Score	.02	.06	-.07	.07	.12*	.06	.08	.06	.34**	.06	.14*	.07
Subtypes												
Emotional neglect	.05	.19	-.16	.21	.52**	.19	.20	.19	.38*	.19	-.34	.23
Physical abuse	-.09	.18	-.02	.02	-.24	.18	-.27	.18	.16	.19	.30	.21
Psychological abuse	-.19	.20	.05	.23	-.04	.21	.24	.21	.42*	.21	-.01	.24
Sexual abuse	.44	.24	-.04	.27	.58*	.24	.51*	.24	.77**	.24	.31	.26
Violence in the home	.10	.21	-.21	.24	-.14	.21	-.32	.08	.07	.21	.70**	.23

* $p \leq .05$, ** $p \leq .01$

References

- Abramson, A. (2021, March 1). *Substance use during the pandemic*. Monitor on Psychology. Retrieved March 14, 2023, from <https://www.apa.org/monitor/2021/03/substance-use-pandemic>
- Addington, J., Liu, L., Brummitt, K., Bearden, C. E., Cadenhead, K. S., Cornblatt, B. A., Keshavan, M., Mathalon, D. H., McGlashan, T. H., Perkins, D. O., Seidman, L. J., Stone, W., Tsuang, M. T., Walker, E. F., Woods, S. W., & Cannon, T. D. (2022). North American Prodrome Longitudinal Study (NAPLS 3): Methods and Baseline Description. *Schizophrenia Research*, 243, 262–267. <https://doi.org/10.1016/j.schres.2020.04.010>
- Armbruster-Genç, D. J., Valton, V., Neil, L., Vuong, V., Freeman, Z. C., Packer, K. C., Kiffin, M. J., Roiser, J. P., Viding, E., & McCrory, E. (2022). Altered reward and effort processing in children with maltreatment experience: A potential indicator of mental health vulnerability. *Neuropsychopharmacology*, 47(5), 1063–1070. <https://doi.org/10.1038/s41386-022-01284-7>
- Borum, R., Lodewijks, H. P. B., Bartel, P. A., & Forth, A. E. (2020). *Handbook of Violence Risk Assessment* (2nd ed.). Routledge, Taylor & Francis Group.
- Broekhof, R., Nordahl, H. M., Bjørnelv, S., & Selvik, S. G. (2022). Prevalence of adverse childhood experiences and their co-occurrence in a large population of adolescents: A young hunt 3 study. *Social Psychiatry and Psychiatric Epidemiology*, 57(12), 2359–2366. <https://doi.org/10.1007/s00127-022-02277-z>
- Bromfield, L., Lamont, A., Parker, R., & Horsfall, B. (2010, December). *Issues for the safety and wellbeing of children in families with multiple and complex problems*. AIFS. Retrieved March 14, 2023, from <https://aifs.gov.au/resources/policy-and-practice-papers/issues-safety-and-wellbeing-children-families-multiple-and>
- Brown, S. M., Rienks, S., McCrae, J. S., & Watamura, S. E. (2019). The co-occurrence of adverse childhood experiences among children investigated for child maltreatment: A latent class analysis. *Child Abuse & Neglect*, 87, 18–27. <https://doi.org/10.1016/j.chiabu.2017.11.010>
- Busso, D. S., McLaughlin, K. A., Brueck, S., Peverill, M., Gold, A. L., & Sheridan, M. A. (2017). Child abuse, neural structure, and adolescent psychopathology: A longitudinal study. *Journal of the American Academy of Child & Adolescent Psychiatry*, 56(4). <https://doi.org/10.1016/j.jaac.2017.01.013>
- Capistrano, C. G., Bianco, H., & Kim, P. (2016). Poverty and internalizing symptoms: The indirect effect of middle childhood poverty on internalizing symptoms via an emotional response inhibition pathway. *Frontiers in Psychology*, 7. <https://doi.org/10.3389/fpsyg.2016.01242>

- Cawthorpe, D., Marriott, B., Paget, J., Moulai, I., & Cheung, S. (2018). Relationship between adverse childhood experience survey items and psychiatric disorders. *The Permanente Journal*, 22(4). <https://doi.org/10.7812/tpp/18-001>
- Centers for Disease Control and Prevention. (2021, March 4). *Essentials for childhood | Violence Prevention*. Centers for Disease Control and Prevention. Retrieved March 13, 2023, from <https://www.cdc.gov/violenceprevention/childabuseandneglect/essentials/index.html>
- Chandler, G. E., Roberts, S. J., & Chiodo, L. (2015). Resilience intervention for young adults with adverse childhood experiences. *Journal of the American Psychiatric Nurses Association*, 21(6), 406–416. <https://doi.org/10.1177/1078390315620609>
- Cheong, E. V., Sinnott, C., Dahly, D., & Kearney, P. M. (2017). Adverse childhood experiences (ACES) and later-life depression: Perceived social support as a potential protective factor. *BMJ Open*, 7(9). <https://doi.org/10.1136/bmjopen-2016-013228>
- Cheong, E. V., Sinnott, C., Dahly, D., & Kearney, P. M. (2017). Adverse childhood experiences (ACES) and later-life depression: Perceived social support as a potential protective factor. *BMJ Open*, 7(9). <https://doi.org/10.1136/bmjopen-2016-013228>
- Christ, C., de Waal, M. M., Dekker, J. J., van Kuijk, I., van Schaik, D. J., Kikkert, M. J., Goudriaan, A. E., Beekman, A. T., & Messman-Moore, T. L. (2019). Linking childhood emotional abuse and depressive symptoms: The role of emotion dysregulation and interpersonal problems. *PLOS ONE*, 14(2). <https://doi.org/10.1371/journal.pone.0211882>
- Cicchetti, D., & Toth, S. L. (2016). Child maltreatment and developmental psychopathology: A multilevel perspective. *Developmental Psychopathology*, 1–56. <https://doi.org/10.1002/9781119125556.devpsy311>
- Crouch, E., Radcliff, E., Strompolis, M., & Srivastav, A. (2018). Safe, stable, and nurtured: Protective factors against poor physical and mental health outcomes following exposure to adverse childhood experiences (aces). *Journal of Child & Adolescent Trauma*, 12(2), 165–173. <https://doi.org/10.1007/s40653-018-0217-9>
- Dennison, M. J., Rosen, M. L., Sambrook, K. A., Jenness, J. L., Sheridan, M. A., & McLaughlin, K. A. (2017). Differential associations of distinct forms of childhood adversity with neurobehavioral measures of reward processing: A developmental pathway to depression. *Child Development*, 90(1). <https://doi.org/10.1111/cdev.13011>

- Dias, P. C., & Cadime, I. (2017). Protective factors and resilience in adolescents: The mediating role of self-regulation. *Psicología Educativa*, 23(1), 37–43. <https://doi.org/10.1016/j.pse.2016.09.003>
- Drill, R., Nakash, O., DeFife, J. A., & Westen, D. (2015). Assessment of clinical information. *Journal of Nervous & Mental Disease*, 203(6), 459–462. <https://doi.org/10.1097/nmd.0000000000000300>
- Evans, G. W., Li, D., & Whipple, S. S. (2013). Cumulative risk and child development. *Psychological Bulletin*, 139(6), 1342–1396. <https://doi.org/10.1037/a0031808>
- Gama, C. M., Portugal, L. C., Gonçalves, R. M., de Souza Junior, S., Vilete, L. M., Mendlowicz, M. V., Figueira, I., Volchan, E., David, I. A., de Oliveira, L., & Pereira, M. G. (2021). The invisible scars of emotional abuse: A common and highly harmful form of childhood maltreatment. *BMC Psychiatry*, 21(1). <https://doi.org/10.1186/s12888-021-03134-0>
- Gardner, M. J., Thomas, H. J., & Erskine, H. E. (2019). The association between five forms of child maltreatment and depressive and anxiety disorders: A systematic review and meta-analysis. *Child Abuse & Neglect*, 96, 104082. <https://doi.org/10.1016/j.chiabu.2019.104082>
- Green, J. G., McLaughlin, K. A., Berglund, P. A., Gruber, M. J., Sampson, N. A., Zaslavsky, A. M., & Kessler, R. C. (2010). Childhood adversities and adult psychiatric disorders in the national comorbidity survey replication I. *Archives of General Psychiatry*, 67(2), 113. <https://doi.org/10.1001/archgenpsychiatry.2009.186>
- Hamby, S., Grych, J., & Banyard, V. (2018). Resilience portfolios and poly-strengths: Identifying protective factors associated with thriving after adversity. *Psychology of Violence*, 8(2), 172–183. <https://doi.org/10.1037/vio0000135>
- Henry, L. M., Gracey, K., Shaffer, A., Ebert, J., Kuhn, T., Watson, K. H., Gruhn, M., Vreeland, A., Siciliano, R., Dickey, L., Lawson, V., Broll, C., Cole, D. A., & Compas, B. E. (2021). Comparison of three models of adverse childhood experiences: Associations with child and adolescent internalizing and externalizing symptoms. *Journal of Abnormal Psychology*, 130(1), 9–25. <https://doi.org/10.1037/abn0000644>
- Howell, K. H., & Miller-Graff, L. E. (2014). Protective factors associated with resilient functioning in young adulthood after childhood exposure to violence. *Child Abuse & Neglect*, 38(12), 1985–1994. <https://doi.org/10.1016/j.chiabu.2014.10.010>
- Hughes, K., Lowey, H., Quigg, Z., & Bellis, M. A. (2016). Relationships between adverse childhood experiences and adult mental well-being: Results from an

- english national household survey. *BMC Public Health*, 16(1).
<https://doi.org/10.1186/s12889-016-2906-3>
- Janssen, I., Krabbendam, L., Bak, M., Hanssen, M., Vollebergh, W., Graaf, R., & Os, J. (2004). Childhood abuse as a risk factor for psychotic experiences. *Acta Psychiatrica Scandinavica*, 109(1), 38–45. <https://doi.org/10.1046/j.0001-690x.2003.00217.x>
- Jean-Thorn, A., Tremblay-Perreault, A., Dubé, V., & Hébert, M. (2022). A systematic review of community-level protective factors in children exposed to maltreatment. *Trauma, Violence, & Abuse*, 152483802211172.
<https://doi.org/10.1177/15248380221117234>
- Kalin, N. H. (2020). The critical relationship between anxiety and depression. *American Journal of Psychiatry*, 177(5), 365–367.
<https://doi.org/10.1176/appi.ajp.2020.20030305>
- Kalmakis, K. A., & Chandler, G. E. (2013). Adverse childhood experiences: Towards a clear conceptual meaning. *Journal of Advanced Nursing*, 70(7), 1489–1501.
<https://doi.org/10.1111/jan.12329>
- Kelleher, I., Harley, M., Lynch, F., Arseneault, L., Fitzpatrick, C., & Cannon, M. (2008). Associations between childhood trauma, bullying and psychotic symptoms among a school-based adolescent sample. *British Journal of Psychiatry*, 193(5), 378–382.
<https://doi.org/10.1192/bjp.bp.108.049536>
- Kim, Y., Kim, K., Chartier, K. G., Wike, T. L., & McDonald, S. E. (2019). Adverse childhood experience patterns, major depressive disorder, and substance use disorder in older adults. *Aging & Mental Health*, 25(3), 484–491.
<https://doi.org/10.1080/13607863.2019.1693974>
- Kuzminskaite, E., Vinkers, C. H., Milaneschi, Y., Giltay, E. J., & Penninx, B. W. J. H. (2022). Childhood trauma and its impact on depressive and anxiety symptomatology in adulthood: A 6-year Longitudinal Study. *Journal of Affective Disorders*, 312, 322–330. <https://doi.org/10.1016/j.jad.2022.06.057>
- Lambert, H. K., King, K. M., Monahan, K. C., & McLaughlin, K. A. (2016). Differential Associations of threat and deprivation with emotion regulation and cognitive control in adolescence. *Development and Psychopathology*, 29(3), 929–940.
<https://doi.org/10.1017/s0954579416000584>
- Larsson, S., Andreassen, O. A., Aas, M., Røssberg, J. I., Mork, E., Steen, N. E., Barrett, E. A., Lagerberg, T. V., Peleikis, D., Agartz, I., Melle, I., & Lorentzen, S. (2013). High prevalence of childhood trauma in patients with schizophrenia spectrum and affective disorder. *Comprehensive Psychiatry*, 54(2), 123–127.
<https://doi.org/10.1016/j.comppsy.2012.06.009>

- Lensch, T., Clements-Nolle, K., Oman, R. F., Evans, W. P., Lu, M., & Yang, W. (2021). Adverse childhood experiences and co-occurring psychological distress and substance abuse among juvenile offenders: The role of protective factors. *Public Health, 194*, 42–47. <https://doi.org/10.1016/j.puhe.2021.02.014>
- LoPilato, A. M., Goines, K., Addington, J., Bearden, C. E., Cadenhead, K. S., Cannon, T. D., Cornblatt, B. A., Mathalon, D. H., McGlashan, T. H., Seidman, L., Perkins, D. O., Tsuang, M. T., Woods, S. W., & Walker, E. F. (2019). Impact of childhood adversity on corticolimbic volumes in youth at Clinical High-risk for psychosis. *Schizophrenia Research, 213*, 48–55. <https://doi.org/10.1016/j.schres.2019.01.048>
- Matheson, S. L., Shepherd, A. M., Pinchbeck, R. M., Laurens, K. R., & Carr, V. J. (2012). Childhood adversity in schizophrenia: A systematic meta-analysis. *Psychological Medicine, 43*(2), 225–238. <https://doi.org/10.1017/s0033291712000785>
- McCutchen, C., Hyland, P., Shevlin, M., & Cloitre, M. (2022). The occurrence and co-occurrence of aces and their relationship to mental health in the United States and Ireland. *Child Abuse & Neglect, 129*, 105681. <https://doi.org/10.1016/j.chiabu.2022.105681>
- McLaughlin, K. (2017, April). *The Long Shadow of Adverse Childhood experiences*. American Psychological Association. Retrieved February 2, 2023, from <https://www.apa.org/science/about/psa/2017/04/adverse-childhood>
- McLaughlin, K. A., Greif Green, J., Gruber, M. J., Sampson, N. A., Zaslavsky, A. M., & Kessler, R. C. (2012). Childhood adversities and first onset of psychiatric disorders in a national sample of US adolescents. *Archives of General Psychiatry, 69*(11), 1151. <https://doi.org/10.1001/archgenpsychiatry.2011.2277>
- McLaughlin, K. A., Koenen, K. C., Hill, E. D., Petukhova, M., Sampson, N. A., Zaslavsky, A. M., & Kessler, R. C. (2013). Trauma exposure and posttraumatic stress disorder in a national sample of adolescents. *Journal of the American Academy of Child & Adolescent Psychiatry, 52*(8). <https://doi.org/10.1016/j.jaac.2013.05.011>
- McLaughlin, K. A., Sheridan, M., Humphreys, K. L., Belsky, J., & Ellis, B. J. (2020). The value of dimensional models of early experience: Thinking clearly about concepts and categories. <https://doi.org/10.31234/osf.io/29fmt>
- Meng, X., Fleury, M.-J., Xiang, Y.-T., Li, M., & D'Arcy, C. (2018). Resilience and protective factors among people with a history of child maltreatment: A systematic review. *Social Psychiatry and Psychiatric Epidemiology, 53*(5), 453–475. <https://doi.org/10.1007/s00127-018-1485-2>

- Mineo, L. (2022, June 29). *'shadow pandemic' of domestic violence*. Harvard Gazette. Retrieved March 14, 2023, from <https://news.harvard.edu/gazette/story/2022/06/shadow-pandemic-of-domestic-violence/>
- Nikulina, V., Widom, C. S., & Czaja, S. (2010). The role of childhood neglect and childhood poverty in predicting mental health, academic achievement and crime in adulthood. *American Journal of Community Psychology*, 48(3-4), 309–321. <https://doi.org/10.1007/s10464-010-9385-y>
- Oltean, L.-E., Șoflău, R., Miu, A. C., & Szentágotai-Tătar, A. (2022). Childhood adversity and impaired reward processing: A meta-analysis. *Child Abuse & Neglect*, 105596. <https://doi.org/10.1016/j.chiabu.2022.105596>
- Osório, F. L., Loureiro, S. R., Hallak, J. E., Machado-de-Sousa, J. P., Ushirohira, J. M., Baes, C. V., Apolinario, T. D., Donadon, M. F., Bolsoni, L. M., Guimarães, T., Fracon, V. S., Silva-Rodrigues, A. P., Pizeta, F. A., Souza, R. M., Sanches, R. F., dos Santos, R. G., Martin-Santos, R., & Crippa, J. A. (2019). Clinical validity and intrarater and test–retest reliability of the Structured Clinical Interview for DSM-5 – Clinician Version (SCID-5-CV). *Psychiatry and Clinical Neurosciences*, 73(12), 754–760. <https://doi.org/10.1111/pcn.12931>
- Popovic, D., Schmitt, A., Kaurani, L., Senner, F., Papiol, S., Malchow, B., Fischer, A., Schulze, T. G., Koutsouleris, N., & Falkai, P. (2019). Childhood trauma in schizophrenia: Current findings and Research Perspectives. *Frontiers in Neuroscience*, 13. <https://doi.org/10.3389/fnins.2019.00274>
- Powell, K. M., Rahm-Knigge, R. L., & Conner, B. T. (2020). Resilience Protective Factors Checklist (RPFC): Buffering childhood adversity and promoting positive outcomes. *Psychological Reports*, 124(4), 1437–1461. <https://doi.org/10.1177/0033294120950288>
- Racine, N., Eirich, R., Dimitropoulos, G., Hartwick, C., & Madigan, S. (2020). Development of trauma symptoms following adversity in childhood: The moderating role of protective factors. *Child Abuse & Neglect*, 101, 104375. <https://doi.org/10.1016/j.chiabu.2020.104375>
- Rapsey, C. M., Scott, K. M., & Patterson, T. (2019). Childhood sexual abuse, poly-victimization and internalizing disorders across adulthood and older age: Findings from a 25-year longitudinal study. *Journal of Affective Disorders*, 244, 171–179. <https://doi.org/10.1016/j.jad.2018.10.095>
- Ruby, E., Polito, S., McMahon, K., Gorovitz, M., Corcoran, C., & Malaspina, D. (2014). Pathways Associating Childhood Trauma to the Neurobiology of Schizophrenia. *Frontiers in psychological and behavioral science*, 3(1), 1–17.

- Russotti, J., Warmingham, J. M., Duprey, E. B., Handley, E. D., Manly, J. T., Rogosch, F. A., & Cicchetti, D. (2021). Child maltreatment and the development of psychopathology: The role of developmental timing and chronicity. *Child Abuse & Neglect*, 120, 105215. <https://doi.org/10.1016/j.chiabu.2021.105215>
- Schilling, E. A., Aseltine, R. H., & Gore, S. (2008). The impact of cumulative childhood adversity on Young Adult Mental Health: Measures, models, and interpretations. *Social Science & Medicine*, 66(5), 1140–1151. <https://doi.org/10.1016/j.socscimed.2007.11.023>
- Schnarrs, P. W., Stone, A. L., Salcido, R., Georgiou, C., Zhou, X., & Nemeroff, C. B. (2020). The moderating effect of resilience on the relationship between adverse childhood experiences (aces) and quality of physical and mental health among adult sexual and gender minorities. *Behavioral Medicine*, 46(3-4), 366–374. <https://doi.org/10.1080/08964289.2020.1727406>
- Schäfer, J. L., McLaughlin, K. A., Manfro, G. G., Pan, P., Rohde, L. A., Miguel, E. C., Simioni, A., Hoffmann, M. S., & Salum, G. A. (2022). Threat and deprivation are associated with distinct aspects of cognition, emotional processing, and psychopathology in children and adolescents. *Developmental Science*, 26(1). <https://doi.org/10.1111/desc.13267>
- Sheridan, M. A., Peverill, M., Finn, A. S., & McLaughlin, K. A. (2017). Dimensions of childhood adversity have distinct associations with neural systems underlying executive functioning. *Development and Psychopathology*, 29(5), 1777–1794. <https://doi.org/10.1017/s0954579417001390>
- Simpson, T. L., & Miller, W. R. (2002). Concomitance between childhood sexual and physical abuse and substance use problems. *Clinical Psychology Review*, 22(1), 27–77. [https://doi.org/10.1016/s0272-7358\(00\)00088-x](https://doi.org/10.1016/s0272-7358(00)00088-x)
- Smith, B. W., Dalen, J., Wiggins, K., Tooley, E., Christopher, P., & Bernard, J. (2008). The brief resilience scale: Assessing the ability to bounce back. *International Journal of Behavioral Medicine*, 15(3), 194–200. <https://doi.org/10.1080/10705500802222972>
- Smith, K. E., & Pollak, S. D. (2020). Rethinking concepts and categories for understanding the neurodevelopmental effects of childhood adversity. *Perspectives on Psychological Science*, 16(1), 67–93. <https://doi.org/10.1177/1745691620920725>
- Sosnowski, D. W., Feder, K. A., Astemborski, J., Genberg, B. L., Letourneau, E. J., Musci, R. J., Mojtabai, R., McCall, L., Hollander, E., Loving, L., Maher, B. S., Kirk, G. D., Mehta, S. H., & Sun, J. (2022). Adverse childhood experiences and comorbidity in a cohort of people who have injected drugs. *BMC Public Health*, 22(1). <https://doi.org/10.1186/s12889-022-13369-5>

- Strathearn, L., Giannotti, M., Mills, R., Kisely, S., Najman, J., & Abajobir, A. (2020). Long-term cognitive, psychological, and health outcomes associated with Child abuse and neglect. *Pediatrics*, 146(4). <https://doi.org/10.1542/peds.2020-0438>
- Suliman, S., Mkabile, S. G., Fincham, D. S., Ahmed, R., Stein, D. J., & Seedat, S. (2009). Cumulative effect of multiple trauma on symptoms of posttraumatic stress disorder, anxiety, and depression in adolescents. *Comprehensive Psychiatry*, 50(2), 121–127. <https://doi.org/10.1016/j.comppsy.2008.06.006>
- Vanderbilt-Adriance, E., & Shaw, D. S. (2008). Protective factors and the development of resilience in the context of neighborhood disadvantage. *Journal of Abnormal Child Psychology*, 36(6), 887–901. <https://doi.org/10.1007/s10802-008-9220-1>
- Velleman, R., & Templeton, L. (2007). Understanding and modifying the impact of parents' substance misuse on children. *Advances in Psychiatric Treatment*, 13(2), 79–89. <https://doi.org/10.1192/apt.bp.106.002386>
- W., R. J., Zautra, A. J., & Hall, J. S. (2010). *Handbook of Adult Resilience*. The Guilford Press.
- Walsh, C., MacMillan, H. L., & Jamieson, E. (2003). The relationship between parental substance abuse and child maltreatment: Findings from the Ontario Health Supplement. *Child Abuse & Neglect*, 27(12), 1409–1425. <https://doi.org/10.1016/j.chiabu.2003.07.002>
- Wiens, K., Gillis, J., Nicolau, I., & Wade, T. J. (2020). Capturing risk associated with childhood adversity: Independent, cumulative, and multiplicative effects of physical abuse, sexual abuse, and family violence on mental disorders and suicidality. *The Permanente Journal*, 24(2). <https://doi.org/10.7812/tpp/19.079>
- Windle, G. (2010). What is resilience? A review and concept analysis. *Reviews in Clinical Gerontology*, 21(2), 152–169. <https://doi.org/10.1017/s0959259810000420>
- Wüstner, A., Otto, C., Schlack, R., Hölling, H., Klasen, F., & Ravens-Sieberer, U. (2019). Risk and protective factors for the development of ADHD symptoms in children and adolescents: Results of the longitudinal Bella Study. *PLOS ONE*, 14(3). <https://doi.org/10.1371/journal.pone.0214412>
- Zhang, N., Gao, M., Yu, J., Zhang, Q., Wang, W., Zhou, C., Liu, L., Sun, T., Liao, X., & Wang, J. (2022). Understanding the association between adverse childhood experiences and subsequent attention deficit hyperactivity disorder: A systematic review and meta-analysis of observational studies. *Brain and Behavior*, 12(10). <https://doi.org/10.1002/brb3.2748>