

# Research Article

## CHILDHOOD SOCIAL ENVIRONMENT, EMOTIONAL REACTIVITY TO STRESS, AND MOOD AND ANXIETY DISORDERS ACROSS THE LIFE COURSE

Katie A. McLaughlin, Ph.D.,<sup>1,2\*</sup> Laura D. Kubzansky, Ph.D.,<sup>1,3</sup> Erin C. Dunn, M.P.H.,<sup>1</sup> Robert Waldinger, M.D.,<sup>4</sup> George Vaillant, M.D.,<sup>4</sup> and Karestan C. Koenen, Ph.D.<sup>1,3,5</sup>

**Background:** *Adverse child environments are associated with the onset of mood and anxiety disorders in adulthood. The mechanisms underlying these life-course associations remain poorly understood. We investigate whether emotional reactivity to stress is a mechanism in the association between childhood environment characteristics and adult mood and anxiety disorders.* **Methods:** *Data are from the Study of Adult Development, a longitudinal study of men (N = 268) followed for nearly seven decades beginning in late adolescence. Childhood social environment characteristics were assessed during home visits and interviews with respondents' parents at entry into the study. Stress reactivity was assessed during respondents' sophomore year of college via physician exam. Onset of mood and anxiety disorders in adulthood was ascertained by research psychiatrists who completed chart reviews of interview, questionnaire, and physical exam data collected during repeated assessments from age 20 to 70.* **Results:** *Respondents with better overall childhood environments and a greater number of environmental strengths were at lower odds of developing a mood or anxiety disorder in adulthood than respondents with more adverse childhood environments. Higher stress reactivity was observed among respondents from families with lower socio-economic status and with childhood environments characterized by greater conflict and adversity. Elevated stress reactivity, in turn, predicted the onset of adult mood and anxiety disorders.* **Conclusion:** *Heightened emotional reactivity in early adulthood is associated with both adverse childhood environments and elevated risk for developing mood and anxiety disorders in adulthood. Emotional reactivity may be one mechanism linking childhood adversity to mood and anxiety disorders in adulthood.* *Depression and Anxiety 27:1087–1094, 2010.* © 2010 Wiley-Liss, Inc.

**Key words:** *childhood environment; childhood adversity; emotional reactivity; anxiety disorder; mood disorder*

*The authors disclose the following financial relationships within the past 3 years:* Contract grant sponsor: Robert Wood Johnson Foundation; Contract grant number: 053572; Contract grant sponsors: W.T. Grant Foundation; The National Institutes of Health; Contract grant numbers: MH078928; MH070627; MH088074; MH042248; K05-MH00364; AG034554.

\*Correspondence to: Katie A. McLaughlin, Department of Health Care Policy, Harvard Medical School, 180 Longwood Avenue, Boston, MA 02115. E-mail: Katie\_McLaughlin@hms.harvard.edu

Received for publication 23 August 2010; Revised 6 October 2010; Accepted 7 October 2010

DOI 10.1002/da.20762

Published online in Wiley Online Library (wileyonlinelibrary.com).

<sup>1</sup>Department of Society, Human Development, and Health, Harvard School of Public Health, Boston, Massachusetts

<sup>2</sup>Department of Health Care Policy, Harvard Medical School, Boston, Massachusetts

<sup>3</sup>Harvard Center on the Developing Child, Cambridge, Massachusetts

<sup>4</sup>Department of Psychiatry, Brigham and Women's Hospital, Harvard Medical School, Boston, Massachusetts

<sup>5</sup>Department of Epidemiology, Harvard School of Public Health, Boston, Massachusetts

## INTRODUCTION

Exposure to adverse childhood experiences, including maltreatment, family instability, and economic hardship, are well-documented risk factors for psychopathology.<sup>[1-3]</sup> The finding that such adversities are associated with elevated risk for disorder onset not only in childhood, but also in adulthood,<sup>[2,3]</sup> suggests that exposure to childhood adversity creates a generalized diathesis to psychopathology that persists across the life-course. One possible explanation for this increased liability to psychopathology is that exposure to stressors early in life impacts the development of the physiological stress response system.<sup>[4-6]</sup> Indeed, dysregulation in physiological systems has been documented among both children<sup>[7-9]</sup> and adults<sup>[10-12]</sup> exposed to psychosocial adversity in childhood. Childhood adversity is also associated with heightened emotional reactivity to stress. Elevated emotional reactivity to daily events has been documented among individuals exposed to maltreatment and other trauma.<sup>[13,14]</sup> Although elevated physiological and emotional reactivity also have been found among children and adults with mood and anxiety disorders,<sup>[4,15-17]</sup> the extent to which such reactivity mediates the association between childhood adversity and adult psychopathology has, to our knowledge, not been examined directly.

Importantly, the particular aspects of childhood environments that lead to maladaptive stress reactivity are poorly characterized. The term childhood adversity is used to describe a wide variety of adverse childhood experiences ranging from poverty to parental instability to maltreatment.<sup>[2]</sup> It may be that only severe adverse events, like abuse, lead to alterations in stress reactivity. Indeed, the preponderance of studies on childhood contributors to stress reactivity have focused on these relatively severe experiences.<sup>[4,10,13,14,18,19]</sup> On the other hand, some evidence suggests that environments characterized by chronic adversity, such as low socioeconomic status and high family conflict, are associated with elevated physiological reactivity.<sup>[7-9,20]</sup> The strength of the association between such environments and maladaptive patterns of stress reactivity may not be as strong as the associations with more severe experiences like abuse. However, the ubiquity of such exposures suggests their role in determining the population-level distribution of psychiatric disorders could be substantial.

Extant evidence on the links between childhood adversity, stress reactivity, and psychiatric disorders has come primarily from cross-sectional studies that examine emotional and physiological responses to laboratory-based stressors.<sup>[11,15,21]</sup> Thus, it remains unclear whether emotional reactivity to stress represents a risk factor for psychopathology or simply a concomitant of current distress. Recent work has attempted to overcome this problem by demonstrating longitudinally that liability to mood and anxiety disorders following stressful life events in adulthood is heightened among individuals who have

experienced childhood adversities.<sup>[18,19,22]</sup> These studies have assumed that a stronger association between adult stress and psychopathology is indicative of greater emotional and physiological reactivity, though reactivity was not measured directly. We are unaware of prospective research directly examining the association between emotional reactivity and the later onset of psychopathology.

The current study examines the associations between the childhood social environment, adolescent emotional reactivity to stress, and the subsequent onset of mood and anxiety disorders in adulthood using prospective data from a cohort of healthy young men followed into late life. We first examine the associations between aspects of the childhood environment and emotional reactivity in late adolescence. Second, we examine the association between emotional reactivity and the onset of mood and anxiety disorders in adulthood. Finally, we evaluate whether emotional reactivity is a mechanism underlying the association between adverse childhood environments and the onset of adult psychiatric disorders. Because the sample includes men from relatively privileged backgrounds, we provide a stringent test of the relationship between the childhood social environment and emotional reactivity. If variation in the childhood environment is associated with reactivity in this sample, then the effect of the childhood environment on stress reactivity would be expected to be much greater in the general population.

## METHODS

### SAMPLE

Data come from the Study of Adult Development, a longitudinal cohort of men first interviewed between 1939 and 1942 when they were college sophomores. The sample included 268 men selected by university health services for participation in an intensive multidisciplinary study of health and aging.<sup>[23,24]</sup> Respondents were selected for participation based on the absence of physical and mental health problems during a medical examination at college entrance and based on an evaluation by the university dean indicating they had the potential to become successful adults. All men were White.

At baseline, participants were interviewed by an internist, a psychiatrist, a psychologist, and an anthropologist. Interviews also were conducted with each respondent's parents, and extensive information on family, psychosocial, and medical history was obtained. Following these evaluations, participants were re-interviewed at ages 25, 30, and 50. Beginning at age 45 they completed mailed questionnaires every 2 years and physical examinations every 5 years. Of the original 268 men, 12 dropped out after college and 6 were killed in World War II. These respondents are included in the current analyses because they provided data on childhood environmental factors and stress reactivity before dropping out of the study.

### MEASURES

**Emotional reactivity.** Emotional reactivity to stress was assessed at baseline during a physical examination completed by a physician. A medical professional performed a venipuncture (i.e. inserted a needle into a vein in the arm to collect a blood sample) and

an ear puncture (i.e. inserted a lancet into the ear to collect a blood sample) on each participant. Physicians rated the amount of apprehension participants exhibited before and during each procedure on a 4-point scale: 0 = no apprehension, 1 = mild apprehension, 2 = moderate apprehension, and 3 = marked apprehension. Similar methods have been used to examine physiological and emotional responses to stress in previous studies.<sup>[25,26]</sup> These indicators of emotional reactivity demonstrated adequate internal consistency when summed as a single scale (Cronbach's  $\alpha = 0.67$ ). We used this continuous measure of emotional reactivity in models examining the associations between the childhood environment, reactivity and psychiatric disorders. 16.8% of the sample responded to the ear puncture with at least mild apprehension, and 39.2% responded with at least mild apprehension to the venipuncture. A smaller proportion (7.5%) responded to the venipuncture with moderate or marked apprehension. We also created a dichotomous indicator of high emotional reactivity. Participants (20.2%) who responded with any apprehension to the ear puncture and with moderate or marked apprehension to the venipuncture were coded as having high stress reactivity.

**Childhood social environment.** During the home visit and parental interviews, information was collected on the social class of participants' family of origin. Parental social class was rated on a 5-point scale: 5 = upper, 4 = upper/upper-middle, 3 = upper-middle, 2 = middle, 1 = working class/blue collar. Maternal and paternal educational attainment also was assessed. A dichotomous indicator of parental marital quality (married and low-conflict versus nonmarried and/or high conflict) was created following home visits. Using a combination of information from parent interviews and home visits, two independent raters rated five facets of the men's childhood social environment (family cohesion, respondent's relationship quality with his mother, father, and siblings, and a global impression of the home environment) on a scale from 1 (poor) to 5 (excellent). These scales were summed into a single composite of environmental strengths. Childhood health, temperament (until age 10), and school functioning (academic performance and engagement in extracurricular activities) also were rated on 1–5 scales based on parent interviews, with lower scores indicating poorer functioning. An overall composite of childhood environment quality was created by summing the five indicators of environmental strengths along with the indicators for childhood health, temperament, and school functioning. Inter-rater reliability for the composite childhood environment scales was good ( $r = .71$ ).<sup>[27]</sup> These measures have been described in more detail previously.<sup>[27–29]</sup>

**Psychiatric disorders.** Incident major depressive episodes from ages 20 to 50 years were assessed using the Indicators of Major Depressive Disorder Scale,<sup>[30]</sup> which was designed to assess symptoms of major depression before the development of modern assessment tools. A research psychiatrist reviewed the medical records, interviews, and psychosocial data collected from participants to assess the presence of eight indicators of major depression: (1) self-reported depressed mood for 2 weeks or more; (2) receipt of a diagnosis of depression from a nonstudy clinician; (3) prescription for anti-depressant medication; (4) concentration difficulties; (5) neurovegetative signs of depression; (6) suicide attempt or completion; (7) sustained anhedonia; and (8) psychiatric hospitalization other than for alcohol or drug problems. Participants who met three or more criteria were coded as having experienced a major depressive episode. Twenty-three participants (9.3%) were classified as having major depression ( $M = 5.1$  indicators,  $SD = 1.9$ ).

Anxiety disorders present between ages 20 and 50 years were assessed by a study psychiatrist (G.E.V.), who performed a thorough chart review of all respondents. Individuals who received a diagnosis of anxiety disorder from a clinician or had multiple complaints about anxiety symptoms or repeated use of minor tranquilizers for anxiety

reduction were classified as having an anxiety disorder. Twelve respondents (4.8%) met these criteria; nearly half with an anxiety disorder ( $n = 5$ ; 41.7%) also met criteria for major depression.

At a later point in time, two independent psychiatrists conducted thorough chart reviews of the medical records, interviews, and psychosocial data collected from participants through age 70. Psychiatrists rated whether each participant had met criteria for major depression or an anxiety disorder at some point in adulthood. Twenty-five participants (10.0%) were coded as having major depression or an anxiety disorder. Although this scale overlapped considerably with the two previous measures, we included it here because disorders were coded for an additional 20 years of follow-up. We included the two previous measures because they allowed us to examine differential effects for depression and anxiety.

## ANALYSIS METHODS

To determine whether emotional reactivity explained the association between childhood environmental characteristics and adult psychiatric disorders, we used standard tests of statistical mediation.<sup>[31]</sup> We first examined the associations between childhood environmental characteristics and adult disorders using logistic regression. Second, the associations between the childhood environment and emotional reactivity (continuous measures) were examined using linear regression. Third, the relationships between emotional reactivity and adult psychiatric disorders were examined using logistic regression. We evaluated the degree of attenuation in the association between the childhood environment and adult disorders in the final model to evaluate the hypothesis that emotional reactivity mediates the longitudinal association between adverse childhood environments and adult psychiatric disorders. All 268 men were included in the analysis. Logistic regression coefficients and their standard errors were exponentiated to create odds ratios (ORs) and 95% confidence intervals (CIs). Statistical significance was evaluated using two-sided .05-level tests.

## RESULTS

### DISTRIBUTION OF CHILDHOOD ENVIRONMENTAL CHARACTERISTICS

Although the men in our sample had already achieved a relatively privileged status as late adolescents, we found considerable variability in their childhood social environments (Table 1). Compared to respondents with low emotional reactivity, a higher proportion of respondents with high emotional reactivity had parents whose SES was rated as working class/blue collar or lower-middle class and a lower proportion had childhood environments rated as excellent.

### LONGITUDINAL ASSOCIATIONS BETWEEN THE CHILDHOOD SOCIAL ENVIRONMENT AND PSYCHIATRIC DISORDERS

The overall composite of the childhood environment and the composite of environmental strengths were associated with each psychiatric outcome: major depressive episodes between ages 20 and 50, anxiety disorder between ages 20 and 50, and any mood or anxiety disorder by age 70. Childhood environmental characteristics were most strongly associated with risk of developing an anxiety disorder (Table 2).

**TABLE 1. Distribution of childhood environmental characteristics in the total sample and by emotional reactivity among men ( $N = 268$ ) in the Study of Adult Development<sup>a</sup>**

|   | Total sample<br>( $N = 268$ ) |      | Low emotional<br>reactivity ( $n = 214$ ) |      | High emotional<br>reactivity <sup>b,c</sup> ( $n = 54$ ) |      |
|---|-------------------------------|------|---|------|--|------|
|   | <i>N</i>                      | (%)  | <i>N</i>                                  | (%)  | <i>N</i>   | (%)  |
| <i>Overall childhood environment</i>            |                               |      |   |      |  |      |
| Poor  | 47                            | 17.5 | 38  | 18.8 | 9  | 17.0 |
| Moderate  | 76                            | 27.5 | 56  | 27.7 | 20   | 37.7 |
| Good  | 80                            | 29.9 | 63  | 31.2 | 17   | 32.1 |
| Excellent                                       | 52                            | 19.4 | 45  | 22.3 | 7  | 13.2 |
| <i>Environmental strengths</i>                  |                               |      |   |      |  |      |
| Poor  | 64                            | 23.9 | 54  | 26.7 | 10   | 18.9 |
| Moderate/Good                                   | 130                           | 48.5 | 97  | 48.0 | 33   | 62.3 |
| Excellent                                       | 61                            | 22.8 | 51  | 25.3 | 10   | 18.9 |
| <i>Adaptive functioning</i>                     |                               |      |   |      |  |      |
| Poor  | 75                            | 28.0 | 59  | 29.2 | 16   | 30.2 |
| Moderate/Good                                   | 135                           | 50.4 | 104                                       | 51.5 | 31   | 58.5 |
| Excellent                                       | 45                            | 16.7 | 39  | 19.3 | 6  | 11.3 |
| <i>Maternal educational attainment</i>          |                               |      |   |      |  |      |
| Grade school                                    | 17                            | 6.3  | 13  | 6.3  | 4  | 7.4  |
| High school                                     | 123                           | 45.9 | 103                                       | 49.5 | 20   | 37.0 |
| Post-high school training                       | 30                            | 11.2 | 24  | 11.5 | 6  | 11.1 |
| Attended college                                | 83                            | 31.0 | 62  | 29.8 | 21   | 38.9 |
| Attended graduate school                        | 9                             | 3.4  | 6   | 2.9  | 3  | 5.6  |
| <i>Paternal educational attainment</i>          |                               |      |   |      |  |      |
| No formal education                             | 1                             | 0.4  | 0   | 0    | 1  | 1.9  |
| Grade school                                    | 15                            | 5.6  | 13  | 6.2  | 2  | 3.7  |
| High school                                     | 38                            | 14.2 | 30  | 14.3 | 8  | 14.8 |
| Post-high school Training                       | 14                            | 5.2  | 12  | 5.7  | 2  | 3.7  |
| Graduated college                               | 99                            | 36.9 | 76  | 36.2 | 23   | 42.6 |
| Attended graduate school                        | 97                            | 36.2 | 79  | 37.6 | 18   | 33.3 |
| <i>Parental SES</i>                             |                               |      |   |      |  |      |
| Working class/blue collar                       | 43                            | 16.0 | 30  | 15.2 | 13   | 24.1 |
| Lower middle class                              | 57                            | 21.3 | 43  | 21.7 | 14   | 25.9 |
| Middle class                                    | 104                           | 38.8 | 85  | 42.9 | 19   | 35.2 |
| Upper middle class                              | 39                            | 14.6 | 33  | 16.7 | 6  | 11.1 |
| Upper class                                     | 9                             | 3.4  | 7   | 3.5  | 2  | 3.7  |
| <i>Parental marital quality</i>                 |                               |      |   |      |  |      |
| Married and low conflict                        | 68                            | 25.4 | 53  | 33.3 | 15   | 38.5 |
| Separated/Divorced/Widowed and/or High Conflict | 130                           | 48.5 | 106                                       | 66.7 | 24   | 61.5 |

<sup>a</sup>Columns may not add to 100% due to missing data.

<sup>b</sup>Participants who responded with any apprehension to the ear puncture and with moderate or marked apprehension to the venipuncture were coded as having high emotional reactivity. See *Methods* section for details.

<sup>c</sup>Although highly reactive respondents were somewhat more likely to be from lower SES families and to have poorer overall childhood environments, the distribution of childhood environmental characteristics did not vary significantly as a function of adolescent stress reactivity.

Respondents with better overall childhood environments ( $OR = 0.8, P = .005$ ), a greater number of environmental strengths ( $OR = 0.8, P = .020$ ), and greater adaptive functioning ( $OR = 0.7, P = .006$ ) were at lower odds of developing an anxiety disorder in adulthood than respondents with poorer childhood environments.

### ASSOCIATIONS BETWEEN THE CHILDHOOD SOCIAL ENVIRONMENT AND EMOTIONAL REACTIVITY

We next examined the associations between childhood environmental characteristics and emotional

reactivity (response to ear puncture, venipuncture, and total reactivity) in linear regression analyses. Parental SES was associated with apprehension during the venipuncture ( $\beta = -.3, P = .003$ ) and total reactivity ( $\beta = -.2, P = .010$ ), such that respondents whose parents had higher SES were less likely to be reactive (Table 3). Although none of the remaining associations between childhood environmental characteristics and emotional reactivity were significant, we observed a trend in the expected direction for the overall childhood environment. The global composite of the childhood environment was marginally associated with reactivity to the ear puncture ( $\beta = -1.0, P = .094$ ) and

**TABLE 2. Longitudinal associations of childhood environment characteristics with adult mood and anxiety disorders**

| Childhood environmental characteristic         | Major depression (age 20–50) |            | Anxiety disorder (age 20–50) |            | Any mood or anxiety disorder (age 20–70) |            |
|--|------------------------------|------------|------------------------------|------------|--|------------|
|  | OR                           | 5% CI      | OR                           | 95% CI     | OR                                       | 95% CI     |
| Overall childhood assessment <sup>a</sup>      | 0.9**                        | (0.8, 1.0) | 0.8*                         | (0.6, 0.9) | 0.9*                                     | (0.8, 1.0) |
| Childhood environmental strengths <sup>b</sup> | 0.9**                        | (0.8, 1.0) | 0.8*                         | (0.7, 1.0) | 0.9                                      | (0.8, 1.0) |
| Childhood adaptive functioning <sup>c</sup>    | 1.0                          | (0.8, 1.2) | 0.7*                         | (0.5, 0.9) | 0.7*                                     | (0.5, 0.9) |
| Low parental SES                               | 1.1                          | (0.7, 1.6) | 1.2                          | (0.7, 2.1) | 1.1                                      | (0.7, 1.6) |
| Mother’s education                             | 1.2                          | (0.8, 1.8) | 2.1*                         | (1.2, 3.9) | 1.3                                      | (0.9, 1.9) |
| Father’s education                             | 1.0                          | (0.7, 1.4) | 1.1                          | (0.7, 1.7) | 1.2                                      | (0.8, 1.8) |
| Parent marital status                          | 0.7                          | (0.3, 1.8) | 0.7                          | (0.2, 2.4) | 0.7                                      | (0.3, 1.7) |

\*Significant at the .05 level, two-sided test.

\*\*Significant at the .10 level, two-sided test.

<sup>a</sup>Overall childhood assessment includes indicators of childhood environmental strengths (see below) and indicators of childhood health, temperament, and school functioning.

<sup>b</sup>Childhood environmental strengths includes indicators of family cohesion, relationship quality of the respondent with mother, father, and siblings, and a global impression of the childhood home environment.

<sup>c</sup>Childhood adaptive functioning includes indicators of childhood health, temperament, and school functioning.

**TABLE 3. Associations of childhood environment characteristics with emotional reactivity in late adolescence**

| Childhood environmental characteristic         | Ear puncture |         | Venipuncture |         | Total reactivity |         |
|--|--------------|---------|--------------|---------|------------------|---------|
|  | β            | P-value | β            | P-value | β                | P-value |
| Overall childhood assessment <sup>a</sup>      | -.96**       | .094    | -.54         | .173    | -.44**           | .092    |
| Childhood environmental strengths <sup>b</sup> | -.81         | .233    | -.18         | .697    | -.25             | .420    |
| Childhood adaptive functioning <sup>c</sup>    | -.01         | .397    | -.03         | .154    | -.04             | .178    |
| Low parental socio-economic Status             | -.18         | .211    | -.29*        | .003    | -.17*            | .010    |
| Mother’s education                             | .27**        | .068    | -.03         | .728    | .04              | .551    |
| Father’s education                             | .01          | .939    | .07          | .524    | .04              | .642    |
| Parent marital status                          | -.06         | .437    | .03          | .600    | .01              | .994    |

\*Significant at the .05 level, two-sided test.

\*\*Significant at the .10 level, two-sided test.

<sup>a</sup>Overall childhood assessment includes indicators of childhood environmental strengths (see below) and indicators of childhood health, temperament, and school functioning.

<sup>b</sup>Childhood environmental strengths includes indicators of family cohesion, relationship quality of the respondent with mother, father, and siblings, and a global impression of the childhood home environment.

<sup>c</sup>Childhood adaptive functioning includes indicators of childhood health, temperament, and school functioning.

total reactivity ( $\beta = -.4, P = .092$ ), such that respondents with better childhood environments were less reactive.

**LONGITUDINAL ASSOCIATIONS BETWEEN EMOTIONAL REACTIVITY AND PSYCHIATRIC DISORDERS**

Total emotional reactivity was associated with increased odds of each psychiatric outcome, with 40% increased risk for each unit increase in continuous reactivity and two to three times the odds for highly reactive individuals versus those who were less reactive (Table 4). For example, respondents with greater stress reactivity were at elevated risk of developing a mood or anxiety disorder by age 70 (OR = 1.4,  $P = .047$ ). Although not all effects were significant by

conventional standards, the magnitude of the parameter estimates and consistency of effects across outcomes suggest that lack of significance may be due to low case-counts in the sample.

**FINAL MEDIATION MODELS**

Evidence for statistical mediation requires that the putative mediator be associated with both the predictor and outcome. Emotional reactivity was associated with the overall childhood environment and onset of an anxiety disorder by age 50 and a mood or an anxiety disorder by age 70. We therefore examined two mediation models to determine whether emotional reactivity mediated the association between the overall childhood environment and these outcomes. The association between the childhood environment and

**TABLE 4. Longitudinal associations of emotional reactivity with adult mood and anxiety disorders**

| Emotional reactivity           | Major depression <sup>a</sup> |            | Anxiety disorder <sup>b</sup> |            | Any mood or anxiety disorder <sup>c</sup> |            |
|--------------------------------|-------------------------------|------------|-------------------------------|------------|---|------------|
|                                | OR                            | 95% CI     | OR                            | 95% CI     | OR  | 95% CI     |
| Total reactivity (continuous)  | 1.4**                         | (1.0, 2.0) | 1.4                           | (0.9, 2.2) | 1.4*                                      | (1.0, 2.0) |
| Total reactivity (dichotomous) | 2.0                           | (0.8, 5.1) | 3.0**                         | (0.9, 9.9) | 2.3**                                     | (0.9, 5.7) |

\*Significant at the .05 level, two-sided test.

\*\*Significant at the .10 level, two-sided test.

<sup>a</sup>The incidence of major depressive episodes between the ages of 20 and 50 was assessed using the Indicators of Major Depressive Disorder Scale.

<sup>b</sup>The presence of an anxiety disorder between the ages of 20 and 50 was assessed through chart review by a study psychiatrist.

<sup>c</sup>The presence of major depression or an anxiety disorder between the ages of 20 and 70 was coded by two independent psychiatrists. See *Methods* section for details.

anxiety disorder by age 50 was marginally attenuated and remained significant when continuous emotional reactivity was added to the model (OR = 0.8,  $P = .005$ ). When continuous emotional reactivity was added to the model predicting mood or anxiety disorder by age 70, the association between the overall childhood environment and adult disorder was attenuated by 11.1% (OR = 0.9,  $P = .056$ ).

## DISCUSSION

We investigated whether emotional reactivity in adolescence was associated with childhood environmental characteristics and the onset of mood and anxiety disorders in adulthood. We further evaluated whether emotional reactivity explained the association between the childhood social environment and later mental disorders. Even in this relatively small and privileged sample, we found that aspects of the childhood environment were related to variation in emotional reactivity to stress. Emotional reactivity, in turn, predicted the subsequent onset of mood and anxiety disorders in adulthood. We found some evidence for a mediating role of emotional reactivity in the longitudinal relationship between the childhood environment and adult psychopathology. Findings were somewhat weaker than predicted, most likely because the associations between the childhood environment and reactivity were relatively small in magnitude. Given the nature of our sample, however, these are likely lower-bound estimates.

Our results suggest that childhood environmental characteristics are associated with adolescent reactivity to stress. These findings are broadly consistent with evidence suggesting that childhood adversity is associated with greater physiological reactivity to stress,<sup>[7]</sup> heightened emotional reactivity to daily events<sup>[13,14]</sup> and perceived stress following adult life events.<sup>[32]</sup> We extend this work in several important ways. First, we replicate this association using a behavioral indicator of stress reactivity. Our reactivity measure is relatively simple to administer and could be easily incorporated into existing population-based studies that routinely collect physiological samples (e.g. the National Health and Nutrition Evaluation Survey). Second, we

demonstrate that even fairly typical variation in the childhood environment may influence emotional reactivity to stress and increase risk for psychiatric disorders later in life. Most previous research in this area has focused solely on childhood exposures that are traumatic or severely threatening, such as physical and sexual abuse.<sup>[4,11–14]</sup> Our findings suggest that a much broader range of childhood environments may influence emotional reactivity than has previously been shown to be the case.

These results highlight the importance of understanding *why* childhood social circumstances are associated with later emotional reactivity. One possibility is that adverse childhood environments impact the development of physiological stress response systems,<sup>[6]</sup> indeed, accumulating evidence suggests that childhood adversity is associated with dysregulation in the autonomic nervous system and the hypothalamic-pituitary-adrenal axis.<sup>[8,11,12]</sup> This dysregulation may lead to maladaptive emotional and social functioning. A second possibility is that exposure to childhood adversity hinders the development of adaptive emotion regulation skills.<sup>[33]</sup> Stressful life events and chronic stressors have been shown to increase emotion dysregulation,<sup>[34–36]</sup> anxiety sensitivity,<sup>[37]</sup> and perceptions of threat<sup>[7]</sup> in children and adolescents. Youths who have greater difficulties managing arousal and negative emotions are likely to be more emotionally reactive to environmental stressors, a pattern documented among adults with exposure to childhood adversity.<sup>[13,14]</sup>

To our knowledge, we provide the first prospective evidence that emotional reactivity to stress predicts the subsequent onset of psychiatric disorders. These findings are consistent with evidence from cross-sectional studies documenting an association between dysregulation in physiological stress reactivity among individuals with mood and anxiety disorders.<sup>[4,15,17]</sup> However, previous studies have been unable to determine whether alterations in reactivity are a determinant or concomitant of psychiatric disorders. Our results extend this work by demonstrating that adolescent emotional reactivity is associated with the onset of mood and anxiety disorders in adulthood.

We found some evidence to suggest that emotional reactivity mediated the association between childhood

environmental characteristics and adult psychiatric disorders. These findings may have been less strong due to the small size and restricted nature of our sample and our focus on nontraumatic childhood environments. It is also possible that the strength of the findings is diluted by the lengthy follow-up period. Investigation of emotional reactivity as a mechanism underlying life-course associations between the childhood environment and adult psychiatric disorders in larger samples that assess a broader range of childhood environmental exposures represents an important area for future research.

Several additional limitations should be considered when interpreting the results. First, our sample was small, relatively privileged, and included only White men. Not surprisingly, the prevalence of psychiatric disorders was low, and it is possible that the sorts of childhood environments experienced by the men in our sample differ meaningfully from those in the general population. These sample limitations raise questions about the generalizability of our findings to other populations and highlight the importance of replication in more diverse samples. However, it is worth noting that assessing these relationships in this privileged sample likely resulted in conservative estimates of effects. Second, assessment of the childhood environment was retrospective and the childhood assessments did not include information on more severe environmental exposures such as abuse and other trauma. Because maltreatment and trauma exposure co-occur with many of the adverse environments examined in this study,<sup>[38]</sup> some of the observed associations may reflect the effects of these more severe exposures that, although unmeasured, undoubtedly occurred to some degree in our sample. Caution is warranted in comparing our results with studies focused on maltreatment and trauma. Finally, it is possible that some men developed mood or anxiety problems before the assessment of stress reactivity. The low prevalence of psychopathology in the sample and selection of men with sound mental health at entry into the study suggest this is unlikely, but lack of direct assessment of child psychopathology is nevertheless a limitation. Despite these limitations, we found meaningful variation in the childhood environment that was related to emotional reactivity and psychopathology. Moreover, these limitations are balanced by a prospective design that involved assessment of emotional reactivity before the onset of psychiatric disorders and repeated psychiatric assessments over nearly seven decades. Findings were also consistent across multiple measures and time points.

Variation in the childhood environment is associated with emotional reactivity to stress in late adolescence. Adolescent reactivity, in turn, predicts the subsequent onset of mood and anxiety disorders in adulthood. Heightened emotional reactivity may explain, in part, the life-course associations between adverse childhood environments and psychiatric disorders.

## REFERENCES

1. Gilman SE, Kawachi I, Fitzmaurice GM, Buka L. Socio-economic status, family disruption and residential stability in childhood: relation to onset, recurrence and remission of major depression. *Psychol Med* 2003;33:1341–1355.
2. Green JG, McLaughlin KA, Berglund P, et al. Childhood adversities and adult psychopathology in the National Comorbidity Survey Replication (NCS-R) I: associations with first onset of DSM-IV disorders. *Arch Gen Psychiatry* 2010;62:113–123.
3. Kessler RC, Davis CG, Kendler KS. Childhood adversity and adult psychiatric disorder in the US National Comorbidity Survey. *Psychol Med* 1997;27:1101–1119.
4. Heim C, Nemeroff CB. The role of childhood trauma in the neurobiology of mood and anxiety disorders: preclinical and clinical studies. *Biol Psychiatry* 2001;49:1023–1039.
5. Heim C, Newport DJ, Mletzko T, Miller AH, Nemeroff CB. The link between childhood trauma and depressions: insights from HPA axis studies in humans. *Psychoneuroendocrinology* 2008;33:693–710.
6. Loman MM, Gunnar MR. Early experience and the development of stress reactivity and regulation in children. *Neurosci Biobehav Rev* 2010;34:867–876.
7. Chen E, Matthews K. Cognitive appraisal biases: an approach to understanding the relation between socioeconomic status and cardiovascular reactivity in children. *Ann Behav Med* 2001;3:101–111.
8. Ellis BJ, Essex MJ, Boyce WT. Biological sensitivity to context: II. Empirical explorations of an evolutionary-developmental theory. *Dev Psychopathol* 2005;17:303–328.
9. Essex MJ, Klein MJ, Cho E, Kalin NH. Maternal stress beginning in infancy may sensitize children to later stress exposure: effects on cortisol and behavior. *Biol Psychiatry* 2002;52:776–784.
10. Carpenter LL, Carvalho JP, Tyrka AR, et al. Responses to stress in healthy adults reporting significant childhood maltreatment. *Biol Psychiatry* 2007;2:1080–1087.
11. Heim C, Newport DJ, Heit S, et al. Pituitary-adrenal and autonomic responses to stress in women after sexual and physical abuse in childhood. *J Am Med Assoc* 2000;284:592–597.
12. van der Vegt EJM, van der Ende J, Kirschbaum C, Verhulst FC, Tiemeier H. Early neglect and abuse predict diurnal cortisol patterns in adults: a study of international adoptees. *Psychoneuroendocrinology* 2009;34:660–669.
13. Glaser JP, van Os J, Portegijs PJ, Myin-Germeys I. Childhood trauma and emotional reactivity to daily life stress in adult frequent attenders of general practitioners. *J Psychosom Res* 2006;61:229–236.
14. Wichers M, Schrijvers D, Geschwind N, et al. Mechanisms of gene-environment interactions in depression: evidence that genes potentiate multiple sources of adversity. *Psychol Med* 2009;39:1077–1086.
15. Boyce WT, Quas JA, Abbey A, Smider NA, Essex MJ, Kupfer DJ. Autonomic reactivity and psychopathology in middle childhood. *Br J Psychiatry* 2001;79:144–150.
16. Goldin PR, Manber T, Hakimi S, Canli T, Gross JJ. Neural bases of social anxiety disorder: emotional reactivity and cognitive regulation during social and physical threat. *Arch Gen Psychiatry* 2009;66:170–180.
17. Yehuda R. Biology of posttraumatic stress disorder. *J Clin Psychiatry* 2000;61:14–21.
18. Harkness KL, Bruce AE, Lumley MN. The role of childhood abuse and neglect in the sensitization to stressful life events in adolescent depression. *J Abnorm Psychol* 2006;115:730–741.

19. Kendler KS, Kuhn JW, Prescott CA. Childhood sexual abuse, stressful life events, and risk for major depression in women. *Psychol Med* 2004;34:1475–1482.
20. Kapaku GK, Treiber FA, Davis HC. Relationships among socioeconomic status, stress induced changes in cortisol, and blood pressure in African American males. *Ann Behav Med* 2002;24:320–325.
21. Steptoe A, Marmot M. Psychosocial, hemostatic, and inflammatory correlates of delayed poststress blood pressure recovery. *Psychosom Med* 2006;68:531–537.
22. Hammen C, Henry R, Daley SE. Depression and sensitization to stressors among young women as a function of childhood adversity. *J Consult Clin Psychol* 2000;68:782–787.
23. Heath C. *What People Are*. Cambridge, MA: Harvard University Press; 1945.
24. Vaillant GE. *Adaptation to Life*. Boston: Little Brown; 1977.
25. Girgis A, Shea J, Husband A. Immune and psychological responses to acute venipuncture stress. *Med Sci Res* 1988;16:351–352.
26. Ward MM, Mefford IN, Parker SD, et al. Epinephrine and norepinephrine responses in continuously collected human plasma to a series of stressors. *Psychosom Med* 1983;45:471–486.
27. Vaillant GE. The natural history of male psychological health, II: some antecedents of healthy adjustment. *Arch Gen Psychiatry* 1974;31:15–22.
28. Lee KA, Vaillant GE, Torrey WC, Elder GH. A 50-year prospective study of the psychological sequelae of World War II combat. *Am J Psychiatry* 1995;152:516–522.
29. Waldinger RJ, Vaillant GE, Orav EJ. Childhood sibling relationships as a predictor of major depression in adulthood: a 30-year prospective study. *Am J Psychiatry* 2007;164:949–954.
30. Vaillant GE, Meyer SE, Mukamal K, Soldz S. Are social supports in late midlife a cause or a result of successful aging? *Psychol Med* 1998;28:1159–1168.
31. Kraemer HC, Stice E, Kazdin AE, Offord DR, Kupfer DJ. How do risk factors work together? Mediators, moderators, and independent, overlapping, and proxy risk factors. *Am J Psychiatry* 2001;158:846–848.
32. McLaughlin KA, Conron KJ, Koenen KC, Gilman SE. Childhood adversity, adult stressful life events, and risk of past-year psychiatric disorder: a test of the stress sensitization hypothesis in a population-based sample of adults. *Psychol Med* 2010;40:1647–1658.
33. Repetti RL, Taylor SE, Seeman TE. Risky families: family social environments and the mental and physical health of offspring. *Psychol Bull* 2002;128:330–336.
34. Cicchetti D, Toth TL. Child maltreatment. *Annu Rev Clin Psychol* 2005;1:409–438.
35. McLaughlin KA, Hatzenbuehler ML. Mechanisms linking stressful life events and mental health problems in a prospective, community-based sample of adolescents. *J Adolesc Health* 2009;44:153–160.
36. McLaughlin KA, Hatzenbuehler ML, Hilt LM. Emotion dysregulation as a mechanism linking peer victimization to the development of internalizing symptoms among youth. *J Consult Clin Psychol* 2009;77:894–904.
37. McLaughlin KA, Hatzenbuehler ML. Stressful life events, anxiety sensitivity, and internalizing symptoms in adolescents. *J Abnorm Psychol* 2009;118:659–669.
38. Turner HA, Finkelhor D, Ormrod R. The effect of lifetime victimization on the mental health of children and adolescents. *Soc Sci Med* 2006;62:13–27.