Lifetime Adversity Leads to Blunted Stress Axis Reactivity: Studies from the Oklahoma Family Health Patterns Project

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Background: Can stressful events in early life alter the response characteristics of the human stress axis? Individual differences in stress reactivity are considered potentially important in long-term health and disease; however, little is known about the sources of these individual differences. We present evidence that adverse experience in childhood and adolescence can alter core components of the stress axis, including cortisol and heart rate reactivity.

Methods: We exposed 354 healthy young adults (196 women) to public speaking and mental arithmetic stressors in the laboratory. Stress responses were indexed by self-report, heart rate, and cortisol levels relative to measures on a nonstress control day. Subjects were grouped into those who had experienced 0, 1, or 2 or more significant adverse life events, including Physical or Sexual Adversity (mugged, threatened with a weapon, experienced a break-in or robbery or raped or sexually assaulted by a relative or nonrelative) or Emotional Adversity (separation from biological mother or father for at least 6 months before age 15).

Results: Experience of adversity predicted smaller heart rate and cortisol responses to the stressors in a dose-dependent fashion ($0 > 1 >$ 2 or more events) (F values $= 5.79$ and 8.11, p values $< .004$) for both men and women. This was not explained by differences in socioeconomic status, the underlying cortisol diurnal cycle, or subjective experience during the stress procedure.

Conclusions: The results indicate a long-term impact of stressful life experience on the reactivity of the human stress axis.

Key Words: Cortisol, gender, heart rate, lifetime adversity, mental stress, stress reactivity

Cortisol release during acute stress represents both a mobilization of resources and a homeostatic moderator of the stress response (1). Accordingly, a normal cortisol response is taken as a sign of good systems integrity, and by extension stress responses much larger or smaller than normal might indicate systemic dysregulation with potential health implications (2–5). Although there are large individual differences in responses to psychological stress, the primary contributors to this individual difference factor remain poorly understood (6). Recent studies have suggested that the experience of adverse life events in childhood and adolescence might alter regulation of the hypothalamic-pituitary-adrenocortical axis (HPA) and contribute to increased rates of psychiatric disorders (7–10). However, most studies of early life adversity and altered HPA function have been done on persons with comorbid severe trauma and depression or posttraumatic stress disorder, making it difficult to estimate the effect of adversity independent of potential psychiatric vulnerabilities. Carpenter *et al.* (11,12) have recently shown that blunted stress cortisol responses might occur in otherwise healthy young adults exposed to childhood trauma and maltreatment. In agreement with these findings of diminished response to psychological stress are studies showing diminished reactions to direct endocrine challenges in healthy persons with a history of adversity (13,14). This literature has focused on adversity and the HPA, leaving unanswered the question of the impact of adversity on other components of the stress axis, in particular the cardiovascular system.

The present study examines cortisol and heart rate responses to a standardized psychological stress protocol incorporating simulated public speaking and mental arithmetic challenges (15). The study population included healthy young adults free of psychiatric comorbidities but who had experienced a range of physical and psychological adverse events in childhood and early adolescence.

Methods and Materials

Overview

The Oklahoma Family Health Patterns Project is a study of healthy young adults with and without a family history of alcoholism ($n = 156$ and $n = 198$, respectively). Because of the sample size and consistent protocol, the dataset provides a useful resource for assessing the individual differences in stress reactivity in healthy young adults. In preliminary analyses, family history of alcoholism was not a significant predictor of heart rate or cortisol reactivity when adversity was accounted for (F values < 1.0). We therefore considered the present dataset suitable for examining adversity independent of family history.

Subjects

The sample includes 354 persons (158 men, 196 women) recruited through community advertisement. Each subject signed a consent form approved by the Institutional Review Board of the University of Oklahoma Health Sciences Center and the Veterans Affairs Medical Center in Oklahoma City, Oklahoma, and received financial compensation for participating.

Inclusion and Exclusion Criteria

Prospective volunteers were excluded if they: had a history of alcohol or drug dependence; met criteria for substance abuse

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within the past 2 months; failed a urine drug screen or a breath-alcohol test on days of testing; or had a history of any Axis I disorder other than past depression, as defined by the *Diagnostic and Statistical Manual of Mental disorders, 4th ed.* (16). Women were required to have a negative urine pregnancy test on each day of testing. All participants were in good physical health, had a body mass index <30, were not taking prescription medications, and had no reported history of serious medical disorder. Smoking and smokeless tobacco use were not exclusionary. Preliminary analyses showed no difference in cortisol reactivity between tobacco users and nonusers.

Because cortisol secretion is dependent on the sleep-wake cycle (17), volunteers were required to have a normal work or school schedule and to have a nighttime sleep pattern. Also, because acute cortisol secretion is affected by prevailing blood glucose levels (18), all volunteers ate a standard meal before beginning the protocol.

Subject Background and Psychological Assessments

A preliminary telephone screening was followed by a lab visit for a psychiatric history assessed with the computerized version of the Diagnostic Interview Schedule-IV (C-DIS-IV) (19), conducted by a trained assistant under the supervision of a licensed clinical psychologist and assessment of family history of alcoholism.

Lifetime adversity was based on C-DIS-IV items that were closely similar to the life events assessed retrospectively in the studies by Caspi (20,21) as follows: Physical or Sexual Adversity (Have you ever been mugged or threatened with a weapon? Have you ever experienced a break-in or robbery? Have you ever been raped or sexually assaulted by a relative? Have you ever been raped or sexually assaulted by someone not related to you?) and Emotional Adversity (Before you were 15, was there a time when you did not live with your biological mother for at least 6 months? Before you were 15, was there a time when you did not live with your biological father for at least 6 months?). Each person was assigned an adversity score ranging from 0 (no adverse events) to a maximum of 5. Social status was estimated with Hollingshead's measure of socioeconomic status (SES), defined as the highest occupational level of the head of household in which the subject grew up (22).

Study Design and Procedure

Subjects visited the lab twice for behavioral and psychophysiological testing, and were tested at the same time on both days, either in the morning at 9:00 AM ($n = 169$) or in the afternoon at 1:00 PM ($n = 185$). To maximize stress responses, the first day in the lab involved the stress procedure, and the second day was designated the resting control day. Subjects were briefed in advance of this test order and were told to expect to deliver short speeches and a mental arithmetic task. Placing stress exposure on day 1 is comparable to the use of a single study day as done in most stress research, as discussed previously (23).

Stress Protocol. The stress protocol lasted 75 min, consisting of a 30-min prestress baseline, when the subject sat quietly and read general interest magazines, followed by 45 min of behavioral stress. Stress included simulated public speaking (24) followed by mental arithmetic (15). The speech task (30 min) included three speeches prepared (4 min) and delivered (4 min) with no breaks before a video camera and observed by a white-coated experimenter holding a clipboard as described elsewhere (23). The subject was told that his or her speech would be shown to the laboratory staff and that they would judge the fluency of delivery of the subject and how convincing their speech was. The speech topics included recounting an article on why hair turns gray, presenting a position for or against whether homosexuals should be allowed to adopt children, and responding to an accusation that the subject was shoplifting. The order of speech topics was randomly assigned for each subject.

The 15-min mental arithmetic task consisted of three 5-min periods with no interruption other than brief instructions. At the start of each period, the subject was given a three-digit number (e.g., 298) and told to add the digits (19) and to add that total to the original number (317), to recite the new number aloud, and to proceed in that fashion for 5 min until told to stop. The experimenter monitored the answers and noted errors by telling the subject when an answer was wrong and to start back with their previous correct answer.

Resting Control Day. The protocol lasted 75 min, during which the subject sat and read general interest magazines or watched videotapes of nature programs lacking emotional content.

To assess subjective impact of rest and the stressors, subjects rated their moods at each saliva sample with 12 10-point visual-analogue scales adapted from Lundberg and Frankenhaeuser (25) containing a Distress subscale (impatience, irritability, distress, pleasantness, and control) and an Activation subscale (effort, tension, concentration, interest, and stimulation).

Saliva Collection Times and Cortisol Assay

Saliva samples were collected with the Salivette device (Sarstedt, Newton, North Carolina) and taken at: awakening; arrival at the laboratory; min 10 and 20 of the baseline period; min 15, 30, and 45 of the stress protocol or continued resting protocol; 15 and 30 min after stress or rest; and bedtime. Stress reactivity as reported here was measured at min 10 and 20 of the baseline period and at min 30 and 45 of the stress period contrasted with samples taken at the same times during the extended resting protocol.

Salivettes were centrifuged at 4200 RPM for 20 min. The saliva was transferred to cryogenic storage tubes and placed into a $-20°$ C freezer until shipping. Saliva-free cortisol assays were conducted by Salimetrics (State College, Pennsylvania) with a competitive enzymatic immunoassay (26) with a sensitivity of $<.083$ μg/dL and an interassay coefficient of variation of $<6.42\%$.

In preliminary analyses on cortisol data in the women, no differences were seen in the effect of adversity between the luteal and follicular groups ($t = .71$, $p > .48$). Similarly, women using oral birth control did not differ from those not doing so ($t = .30$, $p = .76$). Menstrual cycle and oral contraceptive effects were accordingly not considered in the subsequent analyses.

Heart Rate

Heart rate was measured from readings made every 2 min with an oscillometric monitor (Dinamap, V100, General Electric, Waukesha, Wisconsin). These were made continuously during both days during the entire period of the protocol. Heart rate data were unavailable for eight subjects due to recording failures.

Data Analysis

Dependent variables were the cortisol and heart rate responses to stress. Cortisol response was measured as the value at the end of the stress period on the stress day minus the comparable value on the resting control day (23). Heart rate was measured as the mean heart rate during speech preparation periods minus the heart rate during the rest day protocol. This avoided confounding the heart rate data by vocal activity during the speech delivery or mental arithmetic answers. Data were analyzed with SAS software (version 9.2 for Windows, SAS Institute, Cary, North Carolina).

Table 1. Subject Demographic and Biometric Characteristics

	Men				Women			
	0	1	>1	*p*	0	1	>1	*p*
N	85	45	28		79	77	40	
Age (yrs)	23.5 (.3)	23.7 (.5)	24.6 (.7)	.1	23.1 (.3)	23.5 (.4)	24.6 (.5)	.01
BMI (Kg/m^2)	23.8 (.4)	24.4 (.6)	25.4 (1.0)	.1	23.0 (.5)	23.3 (.5)	25.0 (1.2)	.06
Education (yrs)	15.8 (.1)	15.2 (.2)	15.0 (.3)	.03	15.6 (.2)	15.3 (.2)	14.8 (.2)	.01
SES	48 (1.5)	48 (1.9)	49 (2.4)	.7	49 (1.5)	44 (1.6)	38 (2.0)	.0001
Race (% White)	89	91	71	.006	89	83	75	.4
Smokers (%) (*n*)	9 (8)	16 (7)	14 (4)	.5	10 (8)	9 (7)	18 (7)	.4
AUDIT	4.0 (.33)	4.4 (.63)	3.6 (.69)	.78	3.3 (.3)	3.6 (.3)	2.7 (.4)	.42
Alcohol Use (oz/mo)	53 (4.84)	52 (6.89)	45 (7.34)	.39	40 (3.89)	46 (3.6)	47 (7.11)	.27
Fam Hx + (%)	25	40	74	.0001	21	60	85	.0001

Entries show mean (SEM) or percentage of total. *P* values are based on *F* tests or *t* statistic.

AUDIT, Alcohol Use Disorders Identification Test; BMI, body mass index; Fam Hx +, positive parental history of alcoholism; oz/mo, ounces/month; SES, Hollingshead socioeconomic status index.

Results

Demographic data are shown in Table 1. Persons with more lifetime adversity had less education and, among women, had lower SES and higher body mass index. Alcohol intake patterns did not differ across adversity groups, among either men or women, *p* values $\geq$ .27. Persons with a family history of alcoholism reported more adverse life events than persons from nonalcoholic families among both men and women.

The psychological impact of the stressors was validated by greater self-reports of activation and distress on the stress day compared with the rest day (Table 2) [Day $\times$ Period, $F(1,343) = 44$, and $F(1,343) = 14.3$, respectively, *p* values $\leq$ .0001]. There were comparable changes over time in reports of activation and distress on both days in both sexes, as indexed by nonsignificant Sex $\times$ Day $\times$ Period interaction terms [$F(1,343) < 1.0$, *p* = nonsignificant (NS)]. Because subjects were tested in both the morning and afternoon hours, we examined heart rate and cortisol as a function of time of day of testing and found that time of day did not account for a significant portion of the variance in any of the results reported in the following text.

Cortisol values on rest and stress days are shown in Figure S1, left panel, in Supplement 1. Cortisol responses to stress are shown in the top panel of Figure 1 for men and women with 0, 1, or >1 adverse life events. The size of the cortisol response diminished as the number of lifetime adverse events increased [$F(2,348) = 5.79$, $p < .004$]. As expected, women had smaller cortisol responses than men [$F(1,348) = 15.99$, $p < .0001$], although the effect of adversity was similar for men and women as indicated by a nonsignificant Sex $\times$ Adversity interaction [$F(2,348) < 1$, *p* = NS]. An expanded model including family history of alcoholism showed no effect of family history on cortisol reactivity ($F < 1$). Similarly, cortisol responses did not differ for whites and nonwhites ($t = 1.2$, $p = .23$).

Table 2. Reports of Activation and Distress on Rest and Stress Days

	Study Period	
	Before	After
Activation Reports		
Women		
Rest day	2.8 (.121)	2.5 (.110)
Stress day	4.3 (.124)	5.1 (.112)
Men		
Rest day	2.5 (.124)	2.2 (.123)
Stress day	4.0 (.143)	4.8 (.125)
Distress Reports		
Women		
Rest day	2.4 (.077)	2.4 (.073)
Stress day	2.9 (.106)	3.5 (.123)
Men		
Rest day	2.4 (.071)	2.5 (.077)
Stress day	2.6 (.086)	3.2 (.108)

Entries show mean ± SEM.

Heart rate data are shown in Figure S1, right panel, in Supplement 1. The heart rate responses to stress are shown in the lower panel of Figure 1 and demonstrate a similar relationship; responses to psychological stress were smaller in men and women with greater numbers of adverse life events [$F(2,340) = 8.11$, $p < .0004$]. Women and men had similar overall levels of heart rate responses, and there was no Sex $\times$ Adversity interaction (*F* values < 1.45, *p* values >.23). Family history of alcoholism did not account for heart rate response differences across adversity groups ($F < 1$). Whites did not differ from nonwhites in heart rate responses ($t = -.76$, $p = .44$).

Heart rate and cortisol responses were modestly but significantly correlated across all subjects ($r = .29$, $p < .0001$) and for men and women ($r = .32$ and $r = .34$, respectively, *p* values $< .0001$).

We examined whether the type of adversity accounted for the aforementioned results and whether this differed for men and women. Women experienced more total adversity ($\chi^2 = 9.08$, $p = .03$) and more emotional and physical adversity ($\chi^2 = 5.71$ and $\chi^2 = 11.23$, *p* values = .006 and .01, respectively), as seen in Table 3. We therefore carried out analyses of variance (ANOVAs) on cortisol and heart rate reactivity, including Sex $\times$ Emotional adverse events (0, 1, 2 adverse life events) and Sex $\times$ Physical Abuse (0, 1, 2, 3 adverse life events) as independent variables. Reports of emotional adversity were significantly related to smaller cortisol and heart rate responses (*F* values = 4.98 and 6.98, respectively, *p* values $< .008$). In contrast, reports of physical and sexual abuse did not account for a significant alteration in reactivity (*F* values ≤ 2.15, *p* values >.097). Women and men were affected equally by exposure to adversity, because Sex and Sex $\times$ Adverse events terms were nonsignificant. Because low SES might also carry with it greater stress and exposure to forms of adversity, we examined SES in relation to cortisol and heart rate reactivity values and found no relationship (*r* values = .001 and .02, respectively, *p* values >.7).

We next asked whether smaller cortisol responses in persons with greater adversity were due to an altered perception of the stressors. The ANOVAs showed that neither activation nor distress reports during stress exposure differed as a function of degree of

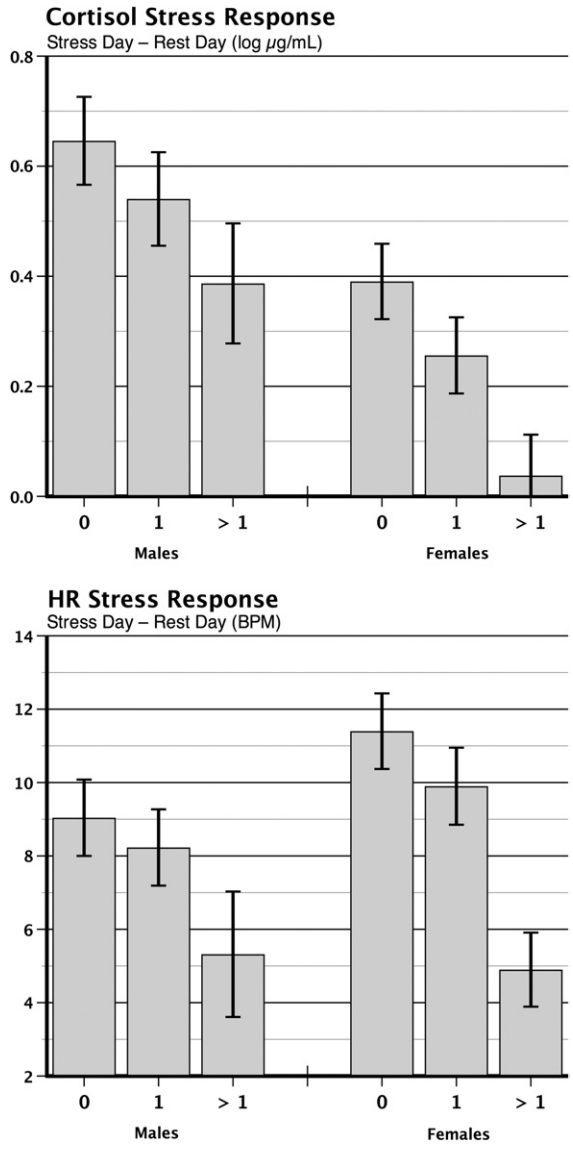

Figure 1. Cortisol responses and heart rate (HR) responses in women and men experiencing three levels of lifetime adversity during childhood and adolescence. BPM, beats per minute.

adversity for men or women, shown by nonsignificant Adversity main effects and Sex × Adversity interaction terms (F values < 1.4, p = NS).

The influence of adversity on cortisol stress reactivity raises the question of whether adversity diminished only stress reactivity or whether nonstress HPA functioning was also affected. An altered diurnal pattern of cortisol secretion would suggest a fundamental shift in the regulation of the HPA as a function of adversity. To assess this, we examined the basal secretion of cortisol in the 10 repeated samples taken across the resting control day, as described in the preceding text and as shown in Figure S2 in Supplement 1, with a Sex × Adversity × Period repeated measure ANOVA. There was a significant effect of period indicating the expected diurnal pattern [$F(9,2667) = 185$, $p < .0001$], but neither sex nor adversity accounted for any differences in diurnal secretion across rest day samples (F values = .00 and .22, respectively, p values = NS), and there were also no sex or adversity interactions with period (F values $< .13$, p values = NS).

Discussion

The present study shows that men and women who experience more adverse life events before age 15 also have smaller cortisol and heart rate responses to psychological stress. These findings seem to illustrate an impact of stress exposure in childhood and adolescence on the regulation of the stress axis in adulthood.

Caspi *et al.* (20,21) demonstrated the deleterious effect of childhood maltreatment on psychiatric and behavioral outcomes in persons with genetic vulnerabilities. Other studies have shown that early adversity might alter HPA reactivity. However, most studies focused on persons with psychiatric diagnoses, including major depression, substance dependence, or posttraumatic stress disorder. These comorbidities all have known endocrine effects, making it difficult to isolate the independent contribution of adversity. In addition to the present study, other studies in healthy adults also show reduced cortisol stress reactivity in persons with early life adverse experiences (11,12,27,28). A related study found blunted cortisol reactivity in 12- to 16-year-old girls exposed to childhood maltreatment (29). One study found no relationship (30). The present study generalizes these findings to encompass another main arm of the stress axis, the autonomic nervous system, which controls heart rate response during stress. Future analyses of heart rate response to stress in relation to adversity should include beat-to-beat variability measures, to examine joint sympathetic and parasympathetic influences in different adversity groups.

We ruled out alterations in the intrinsic regulation of the HPA by observing normal diurnal secretion curves for the three adversity groups on a day with no stress (Figure S2 in Supplement 1). Others have also reported no effects of early adversity on basal secretion across the day (14). These findings suggest that exposure to adverse life events might alter the reactivity of the HPA to descending inputs associated with psychological stressors while leaving intrinsic regulation unaltered. We suspect the same for heart rate regulation, because the adversity groups did not differ in resting heart rates. We also considered the possibility that persons exposed to greater adversity might have diminished psychological reactions to the stressors we used. However, the subjects in all three groups gave similar reports of subjective distress and activation at each saliva collection, which tends to rule out blunted emotional reactions as a cause of the diminished physiological responses. This suggests that the reactivity differences might originate in brain regions conveying the impact of a given psychological reaction to

Table 3. Adverse Events Reports

	Women	Men
Total Events		
0	41 (79)	54 (85)
1	39 (77)	28 (45)
2	13 (28)	15 (23)
3>	7 (14)	3 (5)
Emotional Adverse Events		
0	58 (114)	70 (111)
1	30 (58)	22 (35)
2	12 (24)	8 (12)
Physical and Sexual Abuse		
0	71 (139)	70 (111)
1	23 (45)	30 (47)
2	4.5 (9)	0 (0)
3	1.5 (3)	0 (0)

Entries show % (*n*) of persons reporting each number and type of lifetime events. Total events, $\chi^2 = 9.08$, $p = .03$; emotional adverse events, $\chi^2 = 5.71$, $p = .006$; physical and sexual abuse, $\chi^2 = 11.23$, $p = .01$.

the output systems regulated by the hypothalamus and brainstem. One candidate for this level in the central nervous system includes the anterior cingulate gyrus and basal forebrain, including the hippocampus, amygdala, bed nucleus of the stria terminalis, and nucleus accumbens. The hippocampus and amygdala are both involved in HPA regulation and also play significant roles in shaping responses to external stimuli through their mutual declarative memory and Pavlovian conditioning histories (31,32). The nucleus accumbens displays considerable plasticity of function on the basis of experience with rewards and punishments (33). A limited neuroimaging literature supports the idea that childhood experience in the form of low SES shapes individual response differences at the level of the amygdala, basal forebrain, and anterior cingulate gyrus (34–36).

A substantial literature in animal models shows that the experience of both nurturing and stressful events in early life can have permanent effects on brain systems controlling stress responsivity (37–42). The results presented here are consistent with this literature as it applies to humans. In addition, these findings agree with recent reports in healthy young adults showing diminished cortisol reactivity in relation to adverse experience in childhood and adolescence (11,12) and extend them to encompass diminished autonomic responsivity. At a clinical level, reduced cortisol and autonomic responses to stress are in turn associated with externalizing disorders and impulsive tendencies (43,44) and with earlier initiation of sexual activity in men and women (43), findings consistent with a model under which early life events program biological and behavioral adaptations that might have implications for health and behavior.

Other investigators have attempted to parse the influence of specific lifetime adverse experiences, independent of background social status. In our data, diminished cortisol and heart rate responses were associated primarily with emotional adversity, which was identified on the basis of separation from or loss of a biological parent before age 15. Physical abuse, sexual abuse, or exposure to violence did not predict variation in reactivity in our data. In a study by Carpenter *et al.* (12), childhood physical abuse predicted low cortisol reactivity in a sample of women, and in another study reactivity was predicted by emotional neglect in childhood (11). It is likely that variations in these results are due to the specific characteristics of the study sample and the degree to which each type of adversity is represented. There is no consistent evidence that one type of adversity has a differential impact in later life. A question of interest is the impact of stress at different times during development. The questions about lifetime adversity posed in this study covered events up to the time the respondent was 15 years of age, but age of exposure was not obtained in more detail. Therefore we cannot say whether early childhood adversity might have had a differential impact than adversity in late childhood or early adolescence.

A strength of the present study is the sample size, which is relatively large among studies of stress reactivity. By confining our study sample to persons physically healthy and free of psychiatric comorbidities, we are able to generalize our findings to a broad segment of the general population. We also restricted our sample to persons who were nonobese, and our results are therefore not generalizable to obese populations that might also show HPA dysregulation (45–47). The severity and types of adversity covered in our interview are commonly encountered; 55% of the present sample reported one or more adverse life events. As such, the present results might represent many persons, but they might not be generalizable to groups that have been severely traumatized or that meet diagnostic criteria for posttraumatic stress disorder (48,49). A weakness of the present methodology is shared by most studies of adverse life experience in that the data are derived from retrospective self-report. We believe that this concern is mitigated by the relatively low likelihood that the cortisol and heart rate reactivity differences we saw resulted from systematic bias in how the subjects reported on life events. Instead, unreliable recall would be more likely to cause null findings in a study such as this.

In research on stress reactivity and health, it is most commonly assumed that larger stress responses are worse for health outcomes and that smaller responses are better, perhaps even desirable (50–52). However, this view might miss events associated with the low end of the stress response continuum. We have argued elsewhere that stress responses should be viewed as having a normative range and that deviations from the norm in either direction might signal a systems dysregulation with potential health consequences (5,23). This perspective suggests that studies of reactivity and health might benefit from examining persons at both ends of the reactivity continuum. Recent explorations in this direction have revealed that small stress responses, including both autonomic and endocrine indicators, are characteristic of persons at high risk of substance use disorders and persons with greater adiposity indices, poor vaccination response, and depression (4,23,53–55). The present results therefore indicate that one source of reactivity differences that might impact on recruitment of normative cardiovascular and endocrine reactions to psychological challenges is the experience of adverse life events during critical phases of development.

These findings suggest that the experience of adverse events during childhood and adolescence are associated in a dose-response fashion with smaller cortisol and heart rate responses to psychological stress in both men and women. Exposure to adversity therefore seems to be a meaningful source of individual differences in reactivity to psychological stress. The results were found in an otherwise normative, healthy sample of young adults free of psychiatric comorbidities. This finding points to the role of personal experience in shaping the response characteristics of the human stress axis.

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WRL designed the study and details of the protocol. NHF, AJC, and ASV maintained the dataset and analyzed the data. KHS oversaw the assessment procedures and psychiatric interviews. All authors contributed to writing the article and approve of its content.

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Supplementary material cited in this article is available online.

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Lifetime Adversity Leads to Blunted Stress Axis Reactivity: Studies from the Oklahoma Family Health Patterns Project

Supplemental Information

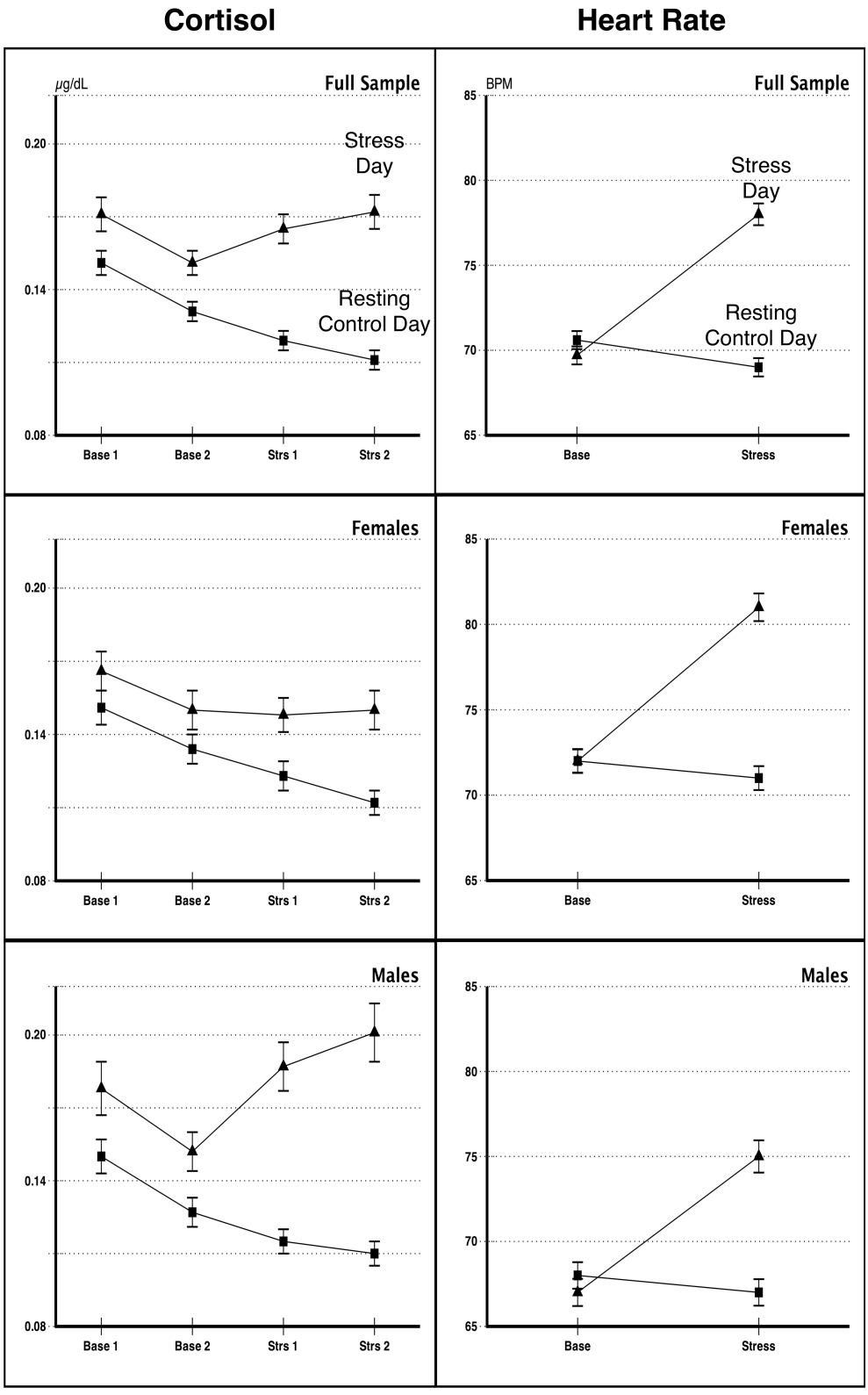

Figure S1. Left Panel shows cortisol on a resting control day and a stress day at two baseline measures and two measures during stress and corresponding rest periods. The effect of the stressor was significant as shown by the Day x Period interaction, F (3, 1050) = 44.83, $p <$ 0.0001. Right Panel shows heart rate on a resting control day and a stress day at averaged over the baseline periods and two speech preparation periods and corresponding rest periods. The effect of the stressor was significant as shown by the Day x Period interaction, F (1, 334) = 317, $p < 0.0001$.

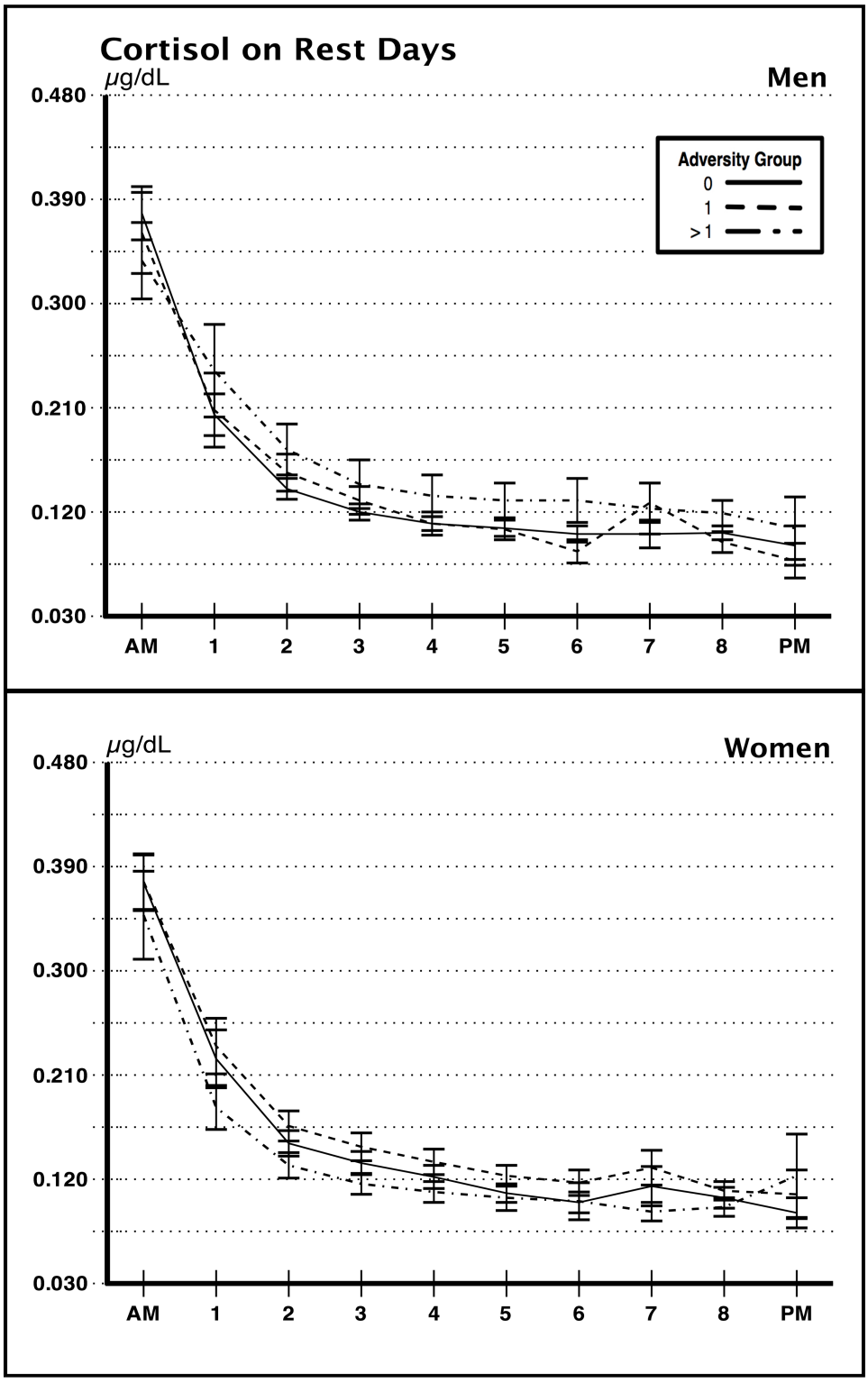

Figure S2. Saliva cortisol at 10 time points on a nonstress control day taken at home upon awakening and on arrival at the lab, and at the following intervals timed to correspond to time points on the stress day protocol: min 10 and 20 of baseline, min 15, 30, and 45 corresponding to the stress protocol, and 15 and 30 min poststress, and at home at bedtime. Analysis showed a

significant diurnal variation in cortisol concentration, F (9, 2667) = 185, $p < .0001$, with no sex or adversity group differences across rest day samples, Fs = 0.00 and 0.22, ps NS, and no sex or adversity interactions with period, Fs < 0.13, ps NS. NS, non-significant.