Health Psychology
2013, Vol. 32, No. 3, 337–344

0278-6133/13/$12.00 DOI: 10.1037/a0028595

Childhood Adversity and Herpesvirus Latency in Breast Cancer Survivors

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Objective: Childhood adversity has been linked to greater emotional and physiological sensitivity to stress. Stress has well-documented effects on cellular immunity, including enhanced herpesvirus reactivation. This study assessed whether childhood adversity was associated with the expression of two latent herpesviruses, Epstein-Barr virus (EBV) and cytomegalovirus (CMV) in adults, and whether this association could be detected beyond the psychological distress women experienced in the aftermath of a breast cancer diagnosis and its treatment. ***Methods:*** One hundred and eight breast cancer survivors completed questionnaires and provided blood samples to assess EBV virus capsid antigen (VCA) IgG antibody titers and CMV IgG antibody titers. ***Results:*** Breast cancer survivors who experienced more childhood adversities had higher EBV and CMV antibody titers than those with fewer childhood adversities. Those who experienced more childhood adversities also had more depressive symptoms, less education, and poorer sleep quality than those with fewer childhood adversities. Depressive symptoms, education, sleep quality, age, BMI, cancer stage, comorbidities, and weekly alcohol consumption were not related to EBV or CMV antibody titers. Time since last treatment was negatively associated with EBV and CMV antibody titers. Elevated antibody titers to latent herpesviruses represent poorer cellular immune system control over viral latency; these data suggest that those with more childhood adversities have poorer cellular immune function. ***Conclusions:*** These findings add to the emerging literature suggesting that adverse early experiences may make people more vulnerable to immune dysregulation in adulthood. The consequences of early adversity appear to persist across the life span.

Keywords: psychoneuroimmunology, stress, cytomegalovirus, Epstein-Barr virus, stressful life events

Childhood adversity has been linked to greater emotional and physiological sensitivity to stress (Hammen, Henry, & Daley, 2000; McLaughlin et al., 2010). For example, people who experienced adversities, as children are more likely to have emotional difficulties when they encounter subsequent stressors in adulthood compared with those who did not have these experiences (Dougherty, Klein, & Davila, 2004). They also have more pronounced stress-induced cortisol and autonomic responses (Heim et al., 2000; Heim, Newport, Mletzko, Miller, & Nemeroff, 2008). Research on latent herpesviruses has provided evidence that stressful early life events may also dysregulate cellular immune function (Dowd, Palermo, & Aiello, 2012; McDade et al., 2000; Shirtcliff, Coe, & Pollak, 2009).

Maladaptive alterations in cellular immune function can enhance herpesvirus reactivation and replication, resulting in elevated herpesvirus antibody titers (Glaser & Kiecolt-Glaser, 1994; Glaser & Kiecolt-Glaser, 2005; Glaser et al., 2005; Steptoe et al., 2007). As an extreme case, organ transplant patients provide a dramatic illustration of the association between dysregulated cellular immune function and elevated herpesvirus antibody titers (Gray et al., 1995). Psychological stress and depression can also dysregulate cellular immunity and enhance herpesvirus reactivation (Glaser & Kiecolt-Glaser, 1994). Although usually asymptomatic, elevated herpesvirus antibody titers reflect poorer cellular immune system control over viral latency (Glaser & Kiecolt-Glaser, 1994).

Adolescents who were abused or institutionalized had higher antibody titers to herpes simplex virus type-1 (HSV-1), reflecting poorer cellular immune system control over the latent virus compared with their contemporaries who were not abused or institutionalized (Shirtcliff et al., 2009). Likewise, adolescent girls who experienced traumatic life events had elevated Epstein-Barr virus (EBV) antibody titers compared with girls who did not experience trauma (McDade et al., 2000). Furthermore, children and adolescents growing up in poverty had elevated cytomegalovirus (CMV) antibody titers compared with those from higher income families

This article was published Online First July 2, 2012.

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Work on this project was supported in part by NIH grants CA131029, CA126857, DE014320, UL1RR025755, and CA016058; the S. Robert Davis endowment; the Kathryn & Gilbert Mitchell endowment; and American Cancer Society Postdoctoral Fellowship Grant PF-11-007-01-CPPB. We thank Cathie Atkinson, Jeanette Bennett, Heather Preston, Mary Lower, and Lindsay Madaras for their helpful assistance. We thank Min Chen for excellent technical assistance in performing the antibody assays.

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(Dowd et al., 2012). Although these studies provide evidence that stressful events early in life can promote herpesvirus reactivation in children and adolescents, we do not know if these same vulnerabilities persist later in life.

Childhood stressors may promote long-term immune system dysregulation. Childhood adversity has been linked to elevated inflammation later in life (Danese et al., 2009; Danese, Pariante, Caspi, Taylor, & Poulton, 2007; Kiecolt-Glaser et al., 2011; Taylor, Lehman, Kiefe, & Seeman, 2006). Older adults who experienced more adversities had shorter telomeres compared with those who experienced fewer adversities (Kiecolt-Glaser et al., 2011). Among basal cell carcinoma patients who experienced a severe stressor in the past year, those who were emotionally maltreated by their parents as children were more likely to have a poorer localized immune response to the tumor (Fagundes et al., in press); these data are consistent with the evidence suggesting that childhood adversity enhances stress sensitivity (Hammen et al., 2000; McLaughlin et al., 2010).

A breast cancer diagnosis and its treatment are notably stressful events, and distress may persist even after treatment completion (Härtl et al., 2003). When treatment-related problems subside, many survivors report quality-of-life difficulties including stress, depressive symptoms, and fear of disease reoccurrence (Ganz et al., 2002; Van den Beuken-van Everdingen et al., 2008). The current study investigated whether childhood adversities were associated with herpesvirus reactivation in adulthood, and whether this association could be detected beyond the psychological distress experienced in the aftermath of breast cancer. We hypothesized that breast cancer survivors who experienced more adversities as children would have elevated EBV and CMV antibody titers compared with those who experienced fewer adversities. Childhood adversity has been linked to depressive symptoms and low socioeconomic status in adulthood (Kessler, Davis, & Kendler, 1997; Poulton et al., 2002), which are both risk factors for maladaptive alterations in immune function (Fagundes, Glaser, et al., 2012; Miller, Freedland, Duntley, & Carney, 2005; Stowe et al., 2010). Accordingly, we examined the possibility that adult depressive symptoms and/or socioeconomic status would mediate relationships between early adversity and antibody titers to EBV and CMV.

Method

Participants

The study data were drawn from the baseline sample of 108 women who participated in a clinical trial addressing the potential benefits of yoga for breast cancer survivors. Participants were recruited through breast cancer clinics and media announcements. Eligible women had completed treatment for stage 0 to stage IIIA breast cancer within the past three years (except for tamoxifen/aromatase inhibitors) and were at least two months after surgery, radiation, or chemotherapy, whichever occurred last. Screening exclusions included a prior history of breast or any other cancer except basal or squamous cell carcinoma, more than five hours a week of vigorous physical exercise, diabetes, uncontrolled hypertension, evidence of liver or kidney failure, and symptomatic ischemic heart disease. Out of the 108 participants enrolled, 104 were EBV seropositive and 56 were CMV seropositive. The institutional review board approved the project; all subjects gave written informed consent prior to participation.

Determination of EBV Virus Capsid Antigen (VCA) IgG Antibody Titers in Plasma

Plasma was stored at −80° C until assayed with Euroimmun EBV ELISA plates that measure EBV VCA antibody titers (Fagundes, Bennett, et al., 2012). CMV IgG antibody titers were also determined using Euroimmun CMV ELISA plates (Morris Plains, NJ). CMV and EBV VCA IgG antibody titers were assessed following the recommended procedure with some modifications (Fagundes, Bennett, et al., 2012). Specifically, for each ELISA plate, three controls that were included in each kit (one positive sample, one negative sample, and three calibrators) were run in duplicate. Plasma samples were initially diluted 1:101 with a dilution buffer according to the recommended protocol provided by the company. Six serial-fold dilutions of each sample were assayed. The last dilution factor with a positive IgG value determined the IgG antibody titer. Calculated viral titers for each sample were plotted and samples were rerun if the end point did not fall within the linear range (± 15%). CMV IgG antibody titers were determined following the same protocol as EBV VCA IgG antibody titers. Only CMV seropositive samples were serially diluted to assess the CMV antibody titer. Antibody titers were treated as continuous variables in all of our analyses, based on the extant literature showing that latent virus reactivation occurs to varying degrees and therefore should be represented as continuous (Glaser & Jones, 1994).

Measures

Participants were asked to indicate if they experienced six types of childhood adversity before they were 17 years old (Kessler & Magee, 1993). The adversities included (a) death of the mother, (b) death of the father, (c) severe parental marital problems, (d) an immediate family member suffering from a mental illness, (e) an immediate family member abusing alcohol, and (f) lack of at least one close relationship with an adult. Because the effects of childhood adversity on adult mental health are known to be additive, a variable reflecting number of adversities was created (Kessler, 1997). Only one person had more than three adversities (they had four adversities); accordingly, they were coded as 3. The results presented below are the same when this person was coded as having four adversities.

The Center for Epidemiological Studies Depression Scale (CES-D) has been used extensively as a brief measure of depressive symptomatology (Basco, Krebaum, & Rush, 1997; Radloff, 1977). Cronbach's alpha was .88. Studies have shown acceptable test–retest reliability and excellent construct validity (Basco et al., 1997). As the CES-D has also distinguished depressed from nondepressed participants in community and clinical samples, discriminative validity appears acceptable as well (Basco et al., 1997).

The Charlson Index was used to assess comorbidities (Charlson, Szatrowski, Peterson, & Gold, 1994). It is a widely used measure of comorbidities developed to reliably index physical conditions that individually or in combination increase risk for mortality. The index lists 19 conditions; each condition has a weight from 1 to 6.

A total score was computed by adding all assigned weights for each chronic condition.

The Pittsburgh Sleep Quality Index global score provided data on sleep quality and sleep disturbances (Buysse, Reynolds, Monk, Berman, & Kupfer, 1989). Higher numbers indicate poorer sleep quality.

Participants answered questions about their age, race, smoking status, and weekly average alcohol consumption. Body mass index (BMI; kg/m^2) was calculated from height and weight data obtained during the visit.

Educational level was used to assess SES, as it is less susceptible to fluctuations than current income (Gorman & Sivaganesan, 2007; Marmot et al., 1998; Winkleby, Jatulis, Frank, & Fortmann, 1992).[1] Women chose from the following education options: less than 7 years, junior high only, some high school, high school graduate, some college, college graduate, or graduate/professional school.

Data concerning breast cancer stage were obtained through the Cancer Registry or electronic medical records. Breast cancer stage takes into account the size of the tumor, whether the cancer is invasive or noninvasive, whether the cancer is in the lymph nodes (and how many lymph nodes are involved), and whether the cancer has spread to other parts of the body (Edge et al., 2010). Importantly, 5-year survival rates are based on cancer stage. Additionally, the work-up recommendations and cancer treatment are dictated by cancer stage according to the National Comprehensive Cancer Network guidelines. For example, if a woman has stage I breast cancer, she is treated with breast-conserving surgery (lumpectomy or partial mastectomy) in most cases. The lymph nodes are then evaluated with a sentinel lymph node biopsy or an axillary lymph node dissection. Radiation is given after breast-conserving surgery. If a woman has stage IIIA breast cancer, she will follow different treatment guidelines. Stage IIIA breast cancer is treated with neoadjuvant chemotherapy (chemotherapy before surgery). This may shrink the tumor enough that a lumpectomy or other breast-conserving surgery may be performed. Otherwise, a mastectomy is performed. She will then have a lymph node biopsy or axillary node dissection. Accordingly, including breast cancer stage in the model provides a very good adjustment for cancer severity and associated treatment.

Analytic Method

Zero-order correlations assessed relationships between EBV antibody titers, CMV antibody titers, childhood adversities, cancer stage, time since treatment, age, BMI, comorbidities, depressive symptoms, and alcohol consumption. In three separate hierarchical linear regression models, we examined relationships between childhood adversities, depressive symptoms, and EBV and CMV reactivation. Only women who were seropositive for EBV were included in the model predicting EBV antibody titers, and only women who were seropositive for CMV were included in the model predicting CMV antibody titers. In the first step of the regression analysis predicting depressive symptoms, we adjusted for age, cancer stage, and time since treatment, based on the extant literature showing relationships between these variables and depressive symptoms (Bardwell et al., 2006; Passik et al., 1998). In the first step of both regression models predicting EBV and CMV antibody titers, we adjusted for age, BMI, cancer stage, time since treatment, comorbidities, weekly alcohol consumption, and sleep quality. Childhood adversities were added in the second step. Tobacco use was not included as a covariate because of the low prevalence of smokers in the sample ($n = 6$). We examined residuals to confirm that they were distributed normally.

In the analyses predicting EBV and CMV antibody titers, we also added depressive symptoms and education to the regression models after inclusion of childhood adversities to determine if these variables potentially mediated the relationship between childhood adversity and CMV and/or EBV antibody titers. If either of the potential mediators (i.e., depressive symptoms or education) was associated with both childhood adversities and EBV or CMV antibody titers (indicating that mediation was possible), we planned to generate 95% bias-correct bootstrap confidence intervals for the indirect effect of the potential mediator using 5,000 bootstrap samples (MacKinnon, Lockwood, Hoffman, West, & Sheets, 2002; MacKinnon, Lockwood, & Williams, 2004). We also examined whether depressive symptoms interacted with childhood adversities in predicting CMV and/or EBV antibody titers.

Results

Sample descriptives are presented in Table 1. Zero-order correlations of all study variables are presented in Table 2. Of note, women who experienced more childhood adversities were less educated and had poorer sleep quality than those with fewer childhood adversities. Table 3 summarizes the analyses that assessed the relationship between childhood adversities and depressive symptoms. In the first step of the regression model, age, cancer stage, and time since treatment were not significantly associated with depressive symptoms. After accounting for these covariates, childhood adversities were positively associated with higher depressive symptoms.

Table 4 summarizes the analyses that assessed the relationships between childhood adversities and EBV and CMV antibody titers. In the first regression model, the relationship between childhood adversities and EBV antibody titers was assessed. Time since last treatment was negatively associated with EBV antibody titers. However, age, BMI, cancer stage, comorbidities, weekly alcohol consumption, and sleep were unrelated to EBV antibody titers. After accounting for these covariates, childhood adversities were positively associated with elevated EBV antibody titers. We then added depressive symptoms and education to the model predicting EBV antibody titers. Childhood adversities remained positively associated with elevated EBV antibody titers ($B = .08$, $p = .05$). Depressive symptoms ($B = .00$, $p = .81$) and education ($B = -.05$, $p = .28$) were unrelated to EBV antibody titers so they could not mediate the relationship between childhood adversities and EBV antibody titers. Finally, we examined whether depressive symptoms interacted with childhood adversities to predict EBV antibody titers; this interaction was nonsignificant ($B = .00$, $p = .36$).

[1] When we replaced education with income to index SES, childhood adversities remained positively associated with elevated EBV antibody titers ($B = .10$, $p = .01$) and income was unrelated to EBV antibody titers ($B = -.05$, $p = .28$). Likewise, childhood adversities remained positively associated with elevated CMV antibody titers ($B = .17$, $p = .02$) and income was unrelated to CMV antibody titers ($B = .05$, $p = .27$).

Table 1
Sample Characteristics

Characteristic	$n = 108$ No.	%
Childhood adversities		
0	44	40.1
1	31	28.7
2	21	19.4
3 or more	12	11.1
Ethnicity		
Asian	2	1.9
Black	8	7.4
White	98	90.7
Marital status		
Single	16	14.8
Married	77	71.3
Separated/Divorced	13	12.0
Widowed	2	1.9
Type of treatment		
Surgery Only	12	11.1
Surgery + Radiation	25	23.1
Surgery + Chemotherapy	27	25.0
Surgery + Radiation + Chemotherapy	44	40.7
Cancer stage		
Stage 0	8	7.4
Stage I	49	45.4
Stage IIA	28	25.9
Stage IIB	13	12.0
Stage IIIA	10	9.3
Months since diagnosis (mean [*SD*])	17.51 (8.05)	
Months since last treatment (mean [*SD*])	11.09 (7.73)	
Body mass index (BMI) (mean [*SD*])	27.41 (5.57)	
Sleep quality (mean [*SD*])	7.12 (3.44)	
Depressive symptoms (mean [*SD*])	10.32 (8.15)	
Age, years (mean [*SD*])	51.59 (9.39)	
Education (years)		
High school	7	
Some college	26	
College or university graduate	34	
Graduate or professional training	41	
Income		
10 K to < 25 K	3	
25 K to < 50 K	15	
50 K to < 75 K	23	
75K to < 100 K	30	
100 K	27	
Unreported	10	

In the next regression analysis, we assessed the relationship between childhood adversities and CMV antibody titers. Time since last treatment was negatively associated with CMV antibody titers. Age, BMI, cancer stage, comorbidities, weekly alcohol consumption, and sleep were not associated with CMV antibody titers. After accounting for these covariates, childhood adversities were positively associated with elevated CMV antibody titers. We then added depressive symptoms and education to the model predicting CMV antibody titers. Childhood adversities remained positively associated with elevated CMV antibody titers ($B = .17$, $p = .04$). Depressive symptoms ($B = .01$, $p = .25$) and education ($B = .00$, $p = .94$) were unrelated to CMV antibody titers so they could not mediate the relationship between childhood adversities and CMV antibody titers. Finally, we examined whether depressive symptoms interacted with childhood adversities to predict CMV antibody titers; this interaction was nonsignificant ($B = .00$, $p = .61$).

Discussion

Breast cancer survivors who experienced more childhood adversities had higher EBV and CMV antibody titers, reflecting poorer cellular immune system control of the latent virus, than those with fewer childhood adversities; they also had higher levels of depressive symptoms. This study, the first to show that childhood adversity is associated with herpesvirus reactivation in adulthood, complements and extends related work with children and adolescents (Dowd et al., 2012; Shirtcliff et al., 2009).

The associations between childhood adversities and herpesvirus reactivation remained significant over and above the distress

Table 2
Correlations Among Study Variables

Variable	1	2	3	4	5	6	7	8	9	11	10
1. EBV (log_{10})											
2. CMV (log_{10})	.22										
3. Childhood adversities	.20**	.25*									
4. Age	−.01	.15	.11								
5. BMI	.05	.14	−.06	.08							
6. Cancer stage	.10	.04	−.18	−.01	−.03						
7. Months since treatment	−.26***	−.28**	.06	.07	.11	−.07					
8. Comorbidities	.01	.03	−.09	.13	.00	.12	.06				
9. Weekly alcohol consumption	−.08	−.09	−.09	.07	−.14	.04	.16	.09			
10. Sleep problems	.06	.11	.26***	.03	.09	−.04	.09	−.10	.13		
11. Depressive symptoms	.11	.22	.17*	−.05	.06	.07	−.02	−.10	.00	.61***	
12. Education	−.19t	−.15	−.24**	−.03	−.19**	−.05	.00	−.12	.21**	.00	−.14

Note. BMI = body mass index; CMV = cytomegalovirus; EBV = Epstein−Barr virus.
* $p < .10$. ** $p < .05$. *** $p < .01$.

women experienced in the aftermath of breast cancer. A number of breast cancer patients experience distress, and in some women, these symptoms can persist for 10 to 20 years after treatment (Ahles et al., 2005; Andrykowski et al., 2002; Epping-Jordan et al., 1999). Chronic stressors can dysregulate cellular immune function. For example, family dementia caregivers had greater HSV-1 antibody titers compared with demographically matched controls (Glaser & Kiecolt-Glaser, 1997).

Childhood adversities predicted herpesvirus reactivation over and above health behaviors, markers of socioeconomic status, and depressive symptoms. This complements work in the broader literature on early adversity and immune function (Hertzman, 1999; Miller, Chen, & Parker, 2011). According to biological embedding models of childhood adversity, stress may dysregulate how certain physiological systems develop during sensitive developmental periods early in life (Miller et al., 2011). Consequently, those who experienced major stressors early in life may be more vulnerable to immune dysregulation in adulthood, regardless of their subsequent mood and behaviors (Miller et al., 2011).

Table 3
Summary of Regression Analyses Predicting Depressive Symptoms

	Depressive symptoms			
Model and variable	*B*	*SE*	*p*	95% CI
Step 1				
Age	−.04	.09	.60	−.21, .12
Cancer stage	.54	.74	.47	−.93, 2.0
Months since treatment	−.01	.10	.91	−.22, .19
r	.09			
F	.28		.84	
df	(3,104)			
Step 2				
Age	−.06	.08	.46	−.23, .10
Cancer stage	.79	.74	.29	−.68, 2.3
Months since treatment	−.02	.10	.85	−.22, .19
Childhood adversities	1.53	.78	.05	−.03, 3.1
Δ*r*	.11			
Δ*F*	3.80		.05	
Δ*df*	1			

We found that childhood adversities predicted *both* EBV and CMV reactivation, even though EBV and CMV antibody titers were only modestly associated with each other. Although EBV and CMV reactivation reflect poorer cellular immune system control over viral latency, they are influenced by different mechanisms. In vivo studies indicate that certain neuroendocrine interactions influence some herpesviruses differently than others (Glaser, Kiecolt-Glaser, Speicher, & Holliday, 1985; Kiecolt-Glaser et al., 1984; Kiecolt-Glaser & Glaser, 1987; Yang et al., 2010). Indeed, latent EBV and CMV had different patterns of reactivation during academic stress and space flight (Matalka, Sidki, Abdul-Malik, & Thewaini, 2000; Mehta & Pierson, 2007).

Although herpesvirus reactivation is asymptomatic and usually benign, elevated antibody titers can promote increases in inflammatory markers such as tumor necrosis factor-alpha (TNF-α), interleukin-6 (IL-6), and C-reactive protein (CRP; Fagundes et al., in press; Harris et al., 1999; Roberts, Haan, Dowd, & Aiello, 2010; Simanek et al., 2011; Stassen, Vega-Córdova, Vliegen, & Bruggeman, 2006; Trzonkowski, Myliwska, Szmit, & Wickiewicz, 2003). Elevated inflammation has been linked to a number of age-related diseases (Steptoe et al., 2007). Indeed, older adults who have chronically elevated proinflammatory cytokines are at greater risk for cancer, cardiovascular disease, type II diabetes, osteoporosis, periodontal disease, and rheumatoid arthritis (Ershler & Keller, 2000; Libby, 2007). Accordingly, these findings may be tapping into one possible mechanism linking childhood adversity to elevated rates of morbidity and mortality from a number of chronic diseases (Anda et al., 2009; Dong et al., 2004; Fuller-Thomson & Brennenstuhl, 2009; Miller et al., 2011).

Women who were more recently treated for breast cancer had higher EBV and CMV antibody titers than those who were treated less recently. This is likely because cancer treatment can diminish cellular immunity (Kuo et al., 2008). Indeed, in one study with cancer patients who were assessed before chemotherapy and then followed through treatment, both CMV IgG antibody titers and CMV viral load in leukocytes rose steeply during chemotherapy (Kuo et al., 2008).

There are a few limitations that should be addressed. First, women in our sample may have been biased when reporting childhood adversities; however, adults typically underreport trou-

Table 4
Summary of Regression Analyses Predicting EBV and CMV Antibody Titers

Model and variable	EBV (log_{10})				CMV (log_{10})			
	B	*SE*	*p*	95% CI	*B*	*SE*	*p*	95% CI
Step 1								
Age	.00	.00	.98	−.01, .01	.01	.01	.27	−.01, .02
BMI	.00	.01	.53	−.01, .02	.01	.01	.20	−.01, .04
Cancer stage	.03	.03	.40	−.04, .10	.02	.06	.68	−.10, .14
Months since treatment	−.01	.01	.01	−.02, −.003	−.02	.01	.03	−.03, −.002
Comorbidities	.03	.11	.82	−.20, .25	−.01	.20	.95	−.42, .39
Weekly alcohol consumption	−.01	.01	.63	−.03, .02	−.00	.20	.90	−.04, .03
Sleep	.01	.01	.40	−.01, .03	.02	.02	.35	−.02, .05
r	.30				.39			
F	1.33		.25		1.25			
df	(7,96)				(7,48)		.30	
Step 2								
Age	.00	.00	.75	−.01, .01	.01	.01	.38	−.01, .02
BMI	.01	.01	.30	−.01, .02	.02	.01	.07	−.002, .04
Cancer stage	.04	.03	.22	−.03, .11	.06	.06	.28	−.05, .18
Months since treatment	−.01	.01	.01	−.02, −.004	−.02	.01	.02	−.03, −.002
Comorbidities	.04	.11	.71	−.18, .26	.08	.20	.70	−.32, .47
Weekly alcohol consumption	.00	.01	.92	−.02, .02	.01	.02	.73	−.03, .04
Sleep	.00	.01	.84	−.02, .02	−.00	.02	.91	−.04, .04
Childhood adversities	.09	.04	.02	.01, .16	.15	.07	.03	.01, .28
Δ*r*	.08				.09			
Δ*F*	5.54		.02		4.77			
Δ*df*	1		1		1			

Note. BMI = body mass index; CMV = cytomegalovirus; EBV = Epstein−Barr virus.

bled early life experiences rather than overreport them (Dill, Chu, Grob, & Eisen, 1991). Our sample was also predominately White; it will be important for future studies to investigate if these findings exist among more diverse samples that also include men. Because a breast cancer diagnosis and its treatment are notably stressful events, it is possible that those who experienced early adversities as children would be at particular risk for immune dysregulation because they are primed to be more stress sensitive. Future work should investigate whether the association between early adversity and herpesvirus reactivation exists in other contexts in order to evaluate the generalizability of the findings. Finally, the current study examined links between early adversity and one marker of immune dysregulation: latent herpesvirus reactivation. Future work would benefit from examining links between early adversity and additional markers of immune dysregulation to provide a more comprehensive understanding of how early adversity dysregulates immune function.

In sum, these findings contribute to the emerging literature suggesting that adverse early experiences may make people more vulnerable to immune dysregulation in adulthood. The consequences of early adversity appear to persist across the life span.

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Received November 23, 2011
Revision received February 2, 2012
Accepted April 11, 2012 ■