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Race/ethnic and socioeconomic differences in stress and immune function in The National Longitudinal Study of Adolescent Health

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ABSTRACT

Stress and immune function may be important mediators of the strong association between social factors and health over the life course, but previous studies have lacked the data to fully explore these links in a population-based sample. This study utilizes data from Waves I—IV of the U.S. National Longitudinal Study of Adolescent Health (Add Health) to test the associations of race/ethnicity and socioeconomic status (SES) with levels of perceived stress and exposure to stressful life events (SLE) among 11,050 adult respondents aged 24—32 in 2008—2009. We further tested whether race/ethnicity and SES were associated with Epstein—Barr Virus (EBV) specific IgG antibodies, an indirect marker of cell-mediated immune function. Finally, we tested whether measures of stress were associated with EBV IgG and whether there was evidence that they explain any associations between race/ethnicity, SES and EBV IgG. We found strong associations between lower SES and higher levels of perceived stress (OR 2.07, 95% CI 1.73—2.48 for < high school vs. college or above) and a high level of stressful life events (OR 7.47, 95% CI 5.59—9.98 for < high school vs. college or above). Blacks had higher odds of a high level of stressful life events compared to whites (OR 2.00, 95% CI 1.63—2.47), but not higher perceived stress (OR 1.11, 95% CI 0.96—1.28). Blacks also had significantly higher EBV levels compared to whites ($\beta = 0.136$, $p < 0.01$), but lower SES was not associated with higher EBV IgG. We found no evidence that stressful life events or perceived stress were associated with EBV IgG in this sample, and thus did not account for racial differences in EBV IgG. These results suggest consistent race/ethnic and SES differences in stressful life events, and confirm race/ethnic differences in markers of immune function that may have health implications across the life course.

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1. Introduction

Stress is hypothesized to be an important determinant of multiple health outcomes as well as a potential mediator of the strong association between social factors and health over the life course (Seeman et al., 2010). Moreover, there is strong evidence that the immune system plays a mediating role in the association between psychosocial stress and health outcomes (Segerstrom and Miller, 2004). Thus far, the majority of population-based studies of stress and biological indicators have come from middle-aged and older populations (Glei et al., 2007; Seeman et al., 1997), with little data available on these interactions earlier in the life course. There is evidence that early environments can model immune system development through nutritional and infectious exposures as well as stress-related neuroendocrine pathways (Coe and Laudenslager, 2007; Fagundes et al., 2013; McDade, 2005).

One approach to investigating immune function in population-based studies is the IgG immune response to herpesviruses, such as Epstein—Barr virus (EBV), herpes simplex virus (HSV), varicella zoster virus (VZV), or cytomegalovirus (CMV) (Glaser and Kiecolt-Glaser, 2005; McDade et al., 2000a,b). These viruses are distinctive because once infected, the host is not able to eliminate the virus. Adequate cell-mediated immune function is required to

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maintain the virus in a dormant (i.e. non-replicating) state (Glaser et al., 1991). However, when immune control is weakened, the virus begins to replicate, which in turn stimulates memory B lymphocytes to increase output of virus-specific IgG antibody (Cacioppo et al., 2002). This results in the seemingly paradoxical observation that increased antibody levels ('titers') reflect poorer immune control (Glaser et al., 1991; Kuo et al., 2008). Thus higher EBV antibodies, one focus of this study, provide an indirect measure of one aspect of cell-mediated immune function (Glaser et al., 1991; Segerstrom and Miller, 2004).

The psychoneuroimmunological literature has found consistent associations between herpesvirus antibody titers and stress-related immune suppression (Glaser and Kiecolt-Glaser, 2005), although these findings are most often measured *via* short-term stressors in specialized populations. In particular, studies that have linked herpesvirus antibodies to stressors include academic stress in medical students and military cadets (Glaser et al., 1999; Sarid et al., 2002), caregiving for a family member with Alzheimer's disease (Glaser and Kiecolt-Glaser, 1997), involvement in a poor quality marriage (Herbert and Cohen, 1993), anticipation of space flight by astronauts (Mehta et al., 2000) and early childhood adversity including institutionalization and physical abuse (Shirtcliff et al., 2009). Elevated EBV antibodies specifically have been associated with chronic psychosocial stress in Samoan adolescents, discrimination-related stress in Latino immigrants in Oregon, and in U.S. adolescents in the Great Smoky Mountains exposed to life strain and traumatic events (McClure et al., 2010; McDade, Stallings, Angold, et al., 2000; McDade et al., 2000). Thus far, the majority of this research has come from small-scale, community-based samples that may not generalize to the broader U.S. population. Previous work using nationally representative data from the National Health and Nutritional Examination Survey (NHANES) cross-sectionally linked markers of socioeconomic status (SES) to elevated antibody titers of a related herpesvirus, cytomegalovirus (CMV) (Dowd and Aiello, 2009; Dowd et al., 2012). With the limited data on chronic or acute stressors available in NHANES, the connection between SES, stress, and impaired immune function was only speculative in these studies. The current study addresses this gap by examining the connections between social factors, stress, and immune function in young adults in a prospective survey.

Exposure to stressors is hypothesized to be patterned by the social environment (Baum et al., 1999), but little recent empirical evidence from the U.S. has explicitly examined this link. Lantz et al. found higher numbers of negative life events and higher ratings of marital, parental, and financial stress for those with less education and income among adults aged 24–64 years in the American's Changing Lives Study (Lantz et al., 2005), while Gryzwacz and colleagues found that adults aged 25–74 with lower levels of education reported *fewer* daily stressors in the National Study of Daily Experiences, but these stressors were more severe (Grzywacz et al., 2004). A small but growing literature suggests that SES may moderate associations between stress and health. Results from an adult German sample found that the association between CMV IgG and psychological stress was strongest in low SES individuals (Rector et al., 2014). Low SES has also been found to predict exaggerated stress reactivity of immune (Brydon et al., 2004) and HPA-axis activity (Gruenewald et al., 2006; Kunz-Ebrecht et al., 2004). The higher frequency or severity of stressors among disadvantaged individuals may deplete their "reserve capacity," leading to an erosion of the ability to cope with stress, which may manifest itself biologically (Gallo and Matthews, 1999). Individuals with the dual burden of socioeconomic disadvantage and race/ethnicity related stressors may be at even greater risk of limited access to psychosocial and material coping mechanisms (Myers, 2009). The idea of impaired coping is consistent with the biological conceptualization of allostatic load (Seeman et al., 2010).

The current study utilizes prospective data from Waves I–IV of the National Longitudinal Study of Adolescent Health (Add Health) to examine the associations between race/ethnicity and SES, stress, and EBV IgG levels. We hypothesized that black and lower SES respondents would report higher levels of perceived stress and a greater number of stressful life events. We also hypothesized that lower SES and black race/ethnicity would be associated with higher EBV IgG levels, and that these associations would be partially explained by higher levels of reported stress.

2. Data and methods

Data come from the National Longitudinal Study of Adolescent Health (Add Health), a longitudinal study of a nationally representative sample of adolescents begun in 1994–1995 and followed through 2008. Four waves of data are available, and the surveys collect data on social, economic, psychological and physical well-being with contextual data on the family, neighborhood, community, school, friendships, peer groups, and romantic relationships. Collection of biological data including EBV antibodies via dried blood spot was expanded in Wave IV to understand the social, behavioral, and biological linkages in health trajectories as the Add Health cohort ages through adulthood (Carolina Population Center). At the time of the Wave IV interview, respondents were between 24 and 32 years old, and included 80.3% of the eligible Wave I in-home sample respondents. Those lost to follow-up since Wave 1 were significantly more likely to be male, Hispanic or Asian, non-US born, and have a parent with less than a high school education. Trained and certified interviewers used a finger prick to obtain whole blood spots that were dried and shipped to the University of Washington Medical Center Immunology Lab, in Seattle WA for analysis. The blood spots were frozen until processing, and then analyzed for Epstein–Barr viral capsid antigen IgG using an adaptation of a previously validated ELISA protocol (McDade et al., 2000). Acceptability of the assay was determined by comparing the EBV optical density concentrations of the quality control samples with their established values. The sensitivity of the EBV assay was 9 AU/ml (arbitrary units per milliliter), the within-assay coefficient of variation was 3.9%, and the between-assay coefficient of variation was 10.2%. EBV concentrations of 162 dried blood spot and paired serum samples were strongly linearly associated (Pearson $r = 0.95$). Additional details of the protocol are available at: http://www.cpc.unc.edu/projects/addhealth/data/guides/add-health-wave-iv-documentation-measures-of-inflammation-and-immune-function (Whitsel et al., 2012). *IRB approved Add Health contracts for restricted data access are in place at both Northwestern University and Stony Brook University.*

2.1. Measures

Because associations between stress and herpesvirus antibody titers depend on having been previously infected, the primary outcome variable in this analysis was EBV IgG antibody titers for those respondents who are EBV seropositive. As Add Health has not yet provided guidance regarding seropositivity cut-offs despite the importance of excluding seronegatives for analysis (Dowd et al., 2013b; Slopen et al., 2013b), we estimated those seropositive as the top 90% of antibody levels for the survey-weighted population based on recent nationally representative estimates from NHANES (Dowd et al., 2013). Continuous EBV antibody levels were logarithmically transformed to normalize the distribution. Sensitivity analyses examining threshold effects for high EBV titers (top 10% and top 25%) as the outcome revealed similar substantive results and are available upon request.

The main social exposures of interest were socioeconomic status (SES) and race/ethnicity. SES was measured using completed education levels (less than a high school degree; high school degree, general equivalency diploma, or vocational training instead of high school; vocational training after high school or some college; college graduate or professional training beyond college) and adult household income, coded categorically as < $35,000; $35,000—62,499; $ $62,500—87,499; and ≥$87,500. A binary indicator for missing current income was included. Adjustment of income by household size was made by including the natural log of household size as a covariate.

Race/ethnicity (white, black, Hispanic, Asian, or other race) was coded as mutually exclusive categories, though respondents may have self-identified as multiple categories. If the respondent answered "yes" to the question "Are you of Hispanic or Latino origin?" that respondent was given a race designation of "Hispanic." If the respondent marked "black or African American" and any other race, they were designated as black or African American, and eliminated from the other marked categories. The process was repeated for the remaining race categories in the following order: Asian, Native American, other, and white.

Stress was measured as perceived stress and both 12-month and lifetime stressful life events (SLE). Since appraisal of stressors is an important contributor to the resulting physiological response (McEwen and Seeman, 1999), it is possible that perceived stress will be more closely tied to immune function than more objective measures. Alternatively, stressful life events occurring at critical development periods could contribute to immune dysregulation in a more persistent way than recent stress (Fagundes et al., 2013). Perceived stress was assessed in Wave 4 with a validated 4-item shortened version of the Cohen Perceived Stress scale (PSS) (Cohen et al., 1983). The items assessed stress in the past two weeks (felt unable to control important things in your life; felt confident about your ability to handle your personal problems; felt that things were going your way; felt difficulties were piling so high that you could not overcome them) using a 5-level response scale. Responses for each of the four items were summed, and total scores ranged from 0 to 16. Scores were then categorized into low (0—3), medium (4—6) and high (7—16) perceived stress, based on approximate tertiles of the data.

SLE was assessed with two indices (lifetime and 12 months), both based on a previously utilized additive index (Adkins, 2009) and modified to reflect additional events reported at Wave IV. The lifetime index summed affirmative responses to questions about specific life events reported at any wave (which varied slightly between waves) including: death of parent or mother/father-figure; death of sibling; injury resulting from suicide attempt; having had a friend or family member commit suicide; having witnessed violence; having been the victim or perpetrator of violence or threat of violence (knife or gun pulled, shot or stabbed, slapped/hit/choked/beaten up); child physical abuse; child sexual abuse; running away from home; expulsion from school; experience of miscarriage, stillbirth, abortion or child death; experience of an unplanned pregnancy; putting a child up for adoption; victim of intimate partner violence; STI diagnosis; experience of combat zone; experience of a firefight in combat; being wounded in combat; killing an enemy in combat; being separated, widowed or divorced; death of a partner; arrest; conviction of a crime; having spent time in jail or prison; having spent time in juvenile detention center; cancer diagnosis, being evicted from residence; exchanging sex for money; having been raped; and having been in a motor vehicle accident. Missing information for any wave was coded = 0 for that wave, and due to overlapping recall periods in different waves, each event was counted a maximum of one time for each respondent.

The 12-month SLE index included the following events occurring in the 12 months prior to the Wave IV interview: mother/father-figure death; sibling death; injury resulting from suicide attempt; friend or family member committed suicide; witnessing violence; victim or perpetrator of violence or threat of violence (knife or gun pulled, shot or stabbed, slapped/hit/choked/beaten up); pregnancy ended in miscarriage, abortion, stillbirth; victim of intimate partner violence; STI diagnosis; cancer diagnosis; arrest; conviction; spent time in jail or prison; or loss of a job; being evicted from residence; experiencing a serious injury; and having been in a motor vehicle accident. Because of the skewed distribution of SLE, for each of these indices, we calculated quartiles of risk and compared individuals in the highest SLE quartiles to all others (>6 events for lifetime SLE, >3 events for 12 month SLE). Results for models using continuous SLE as an exposure or different comparison groups were substantively similar and available upon request.

Additional covariates included body-mass index (BMI) calculated from measured height and weight in Wave IV and acute infection reported in the last month due to their potential association with stress and immune parameters (Visser et al., 2001).

2.2. Statistical analysis

First, ordered logistic regression was used to examine the association of SES and race/ethnicity with the Cohen Perceived Stress scale, and binomial logistic regressions were used to test for factors associated with the highest quartile of stressful life events (lifetime); both sets of analyses were run on the seropositive sample only. Next, we examined the overall associations of SES, race/ethnicity and EBV antibody levels (among seropositives), and individual stress measures and EBV using linear regression models with continuous log(EBV) as the outcome. Previous research has found EBV to be correlated with life events in girls but not in boys (McDade et al., 2000), but gender interaction tests in our sample were not significant and thus all analyses use the combined sample. Based on the hypothesis that disadvantaged individuals may have depleted coping abilities (Gallo and Matthews, 1999), we also tested whether associations between SLE, perceived stress, and EBV were moderated by SES or race/ethnicity using interaction terms. All analyses were conducted with weights to account for the complex survey design.

3. Results

3.1. Sample description

Of the 15,701 individuals interviewed at Wave IV, 14,038 had valid data on EBV IgG levels, 12,690 were EBV seropositive, and 11, 486 of these had non-missing values for covariates and sampling weights. Among this group, an additional 484 respondents were excluded for report of HIV or Hepatitis C infection, or current pregnancy, leaving a final analytical sample of 11,050. Of the study variables, those dropped from the analysis sample were more likely to be black, have higher EBV levels, lower BMI, and were less likely to have attained some college education. Table 1 describes the overall sample characteristics.

3.2. Social factors and perceived and lifetime stress

Lower levels of completed education and household income were strongly associated with increased levels of perceived stress (Table 2). Respondents with less than a high school education had roughly twice the odds of being in a higher perceived stress category compared to those who completed college and above (OR 2.07,

Table 1
Sample characteristics, Add Health, Wave IV, weighted (n = 11,050).

	Mean/percent	Standard error
EBV antibodies (AU/ml)	163.17	1.42
Log (EBV) (AU/ml)	4.94	0.01
Lifetime stressful life events (0—20)	4.72	0.08
0—2 events	29.04	0.90
3—6 events	46.13	0.76
7—10 events	18.25	0.70
11—20 events	6.58	0.46
12 month stressful life events (0—13)	2.08	0.05
0 events	23.36	0.77
1 event	27.05	0.67
2 events	18.52	0.54
3—4 events	18.30	0.64
5 or more events	12.77	0.67
Cohen perceived stress scale	4.85	0.05
Low stress	35.58	0.70
Medium stress	28.19	0.65
High Stress	36.23	0.84
Female	49.62	0.71
Male	50.38	0.71
Age	28.37	0.12
Completed education		
Less than high school	8.95	0.67
High school	18.12	0.94
Some college	44.09	0.89
College and above	28.84	1.61
Income		
Missing	7.14	0.64
<$35,000	20.94	0.94
$35,000—62,499	21.70	0.64
$62,500—87,499	23.13	0.71
>$87,500	27.08	1.03
Race/ethnicity		
White	65.91	2.91
Black	15.47	2.03
Hispanic	12.28	1.76
Asian	3.43	0.83
Other race	2.91	0.32
Active infection past month	3.46	0.27
Body Mass Index (kg/m^2)	28.63	0.12
Household size	3.25	0.04

95% CI 1.73—2.48). Asians reported significantly higher levels of perceived stress compared to whites, while there were no significant differences for blacks or Hispanics compared to whites. Males had lower levels of perceived stress compared to females. As

expected, high lifetime and 12-month SLE were both correlated with increased perceived stress.

Lower levels of education and income were also strongly associated with more reported stressful life events (Table 3). In fully adjusted models, respondents with less than a high school education had 7.47 times (95% CI 5.59—9.98) the odds of falling into the highest quartile of stressful life events compared to college graduates, with a corresponding 3.38 times the odds (95% CI 2.63—4.34) for those who only completed high school. In contrast to perceived stress, males reported a higher number of SLE, with 1.83 times the odds (95% CI 1.62—2.08) of falling into the highest quartile of SLE. Also in contrast to perceived stress, there were no significant differences between Asians and whites in SLE, but blacks had 2.0 times (95% CI 1.63—2.47) the odds of falling into the highest SLE quartile compared to whites in fully adjusted models. Hispanics had 32% higher odds of high SLE (OR 1.32, 95% CI 1.01—1.72) compared to whites.

3.3. Social factors, stress, and EBV antibody levels

Contrary to our hypothesis, we found no associations between SES and EBV IgG (Table 4). These results were robust whether education and income were included individually or together in the model. Race/ethnicity, in contrast, was strongly associated with EBV antibody levels. Specifically, blacks had EBV antibody levels that were 13.6% higher than whites, adjusting for education and income. No significant differences in EBV were found for Asians or Hispanics compared to whites. Neither perceived stress nor lifetime stressors were significantly associated with EBV, and consequently did not account for any racial differences in EBV antibody levels. Furthermore, from interaction tests we found no evidence that SES or race/ethnicity significantly modified associations between stress and EBV, consistent the absence of main effects of SES and stressors.

4. Discussion

This study tested associations between race/ethnicity, SES, stress, and EBV IgG levels in the well-characterized Add Health cohort. We found that adult education and income levels were strong predictors of perceived stress and reported lifetime stressful events at ages 24—32, but adult socioeconomic factors were not consistently associated with reduced control of a latent

Table 2
Ordered logistic regression of characteristics associated with Cohen Perceived Stress Scale.

Add Health Wave IV, weighted (n = 11,050)	(1)	(2)	(3)
	OR (CI)	OR (CI)	OR (CI)
Highest quartile of lifetime stressful life events		1.63** (1.44—1.85)	
Highest quartile of 12 month stressful life events			1.51** (1.33—1.71)
Male	0.69** (0.63—0.76)	0.66** (0.60—0.73)	0.66** (0.60—0.73)
Age	1.02 (0.99—1.05)	1.01 (0.99—1.04)	1.02 (0.99—1.05)
Completed education (ref = college/above)			
Less than high school	2.07** (1.73—2.48)	1.76** (1.47—2.11)	1.87** (1.57—2.24)
High school	1.64** (1.40—1.94)	1.52** (1.29—1.79)	1.57** (1.33—1.85)
Some college	1.39** (1.25—1.55)	1.30** (1.17—1.45)	1.33** (1.20—1.48)
Income (ref=>$87,500)			
<$35,000	2.79** (2.36—3.29)	2.64** (2.22—3.14)	2.71** (2.29—3.21)
$35,000—62,499	1.86** (1.61—2.15)	1.84** (1.59—2.13)	1.86** (1.61—2.15)
$62,500—87,499	1.37** (1.21—1.55)	1.35** (1.20—1.53)	1.36** (1.21—1.54)
Race/ethnicity (ref = white)			
Black	1.11 (0.96—1.28)	1.04 (0.90—1.20)	1.04 (0.90—1.20)
Hispanic	1.01 (0.86—1.19)	0.99 (0.86—1.15)	0.99 (0.84—1.16)
Asian	1.64** (1.32—2.04)	1.67** (1.34—2.09)	1.66** (1.33—2.07)
F-statistic	25.92	30.94	31.2

**p < 0.01, *p < 0.05.
Notes: Robust 95% confidence intervals in parentheses; models also control for "other" race, missing income, recent infection, BMI, and household size.

Table 3
Logistic regression of characteristics associated with highest quartile of lifetime stressful life events.

Add health Wave IV, weighted ($n = 11,050$)	(1)	(2)	(3)
	OR (CI)	OR (CI)	OR (CI)
Male	1.90** (1.69–2.13)	1.70** (1.50–1.93)	1.83** (1.62–2.08)
Completed education (ref = college/above)			
Less than high school		9.75** (7.29–13.04)	7.47** (5.59–9.98)
High school		4.14** (3.22–5.31)	3.38** (2.63–4.34)
Some college		3.39** (2.76–4.16)	3.01** (2.44–3.72)
Income (ref=>$87,500)			
<$35,000			2.16** (1.76–2.66)
$35,000–62,499			1.38** (1.11–1.72)
$62,500–87,499			1.31** (1.09–1.57)
Race/ethnicity (ref = white)			
Black	2.44** (1.99–3.01)	2.25** (1.83–2.77)	2.00** (1.63–2.47)
Hispanic	1.46** (1.13–1.89)	1.30 (0.99–1.72)	1.32* (1.01–1.72)
Asian	0.64** (0.45–0.89)	0.84 (0.59–1.21)	0.87 (0.62–1.22)
F-statistic	30.37	34.95	27.66

$**p < 0.01$, $*p < 0.05$.
Notes: Robust confidence intervals in parentheses; models also control for "other" race, missing income, recent infection, BMI, household size, and age.

herpesvirus, one aspect of cell-mediated immune function. Substantial racial/ethnic differences in EBV levels were seen, with blacks having significantly higher levels compared to whites. These associations were not explained by reported stress, which had no association with EBV IgG levels. These results suggest that while socioeconomic factors strongly predict reported stress, the physiological impact of this stress is not reflected in EBV levels in this young adult sample.

Our findings for SES and EBV contribute to a mixed literature in the association of SES and herpesvirus antibodies. Several previous studies have identified associations between lower SES and higher herpesvirus antibody levels including CMV in the overall U.S. population (Dowd and Aiello, 2009), CMV and HSV-1 in an sample of elderly Latino Americans (Dowd et al., 2008) and for HSV-1 in a community-based sample from Texas (Stowe et al., 2010). Of note, Stowe et al. found that those with higher levels of education had *higher* levels of EBV antibody despite lower levels of HSV-1 antibody in their sample. Recent national estimates from NHANES also

found no significant differences in EBV titers by family SES among children aged 6–19, although elevated EBV antibodies were seen in blacks compared to whites, consistent with our findings (Dowd et al., 2013; Ford and Stowe, 2013). Together these results suggest that the association of SES with EBV may differ from that of other herpes viruses; a result that deserves further investigation.

Previous population-based research has demonstrated race/ethnic differences in the seroprevalence of herpes viruses, with U.S. blacks more likely to be seropositive for EBV, HSV-1, and CMV (Zajacova et al., 2009), but research on race/ethnic differences in herpersvirus antibody levels has been mixed. Blacks were found to have significantly higher CMV levels compared to whites in NHANES III data, with no differences between Mexican-Americans and whites (Dowd and Aiello, 2009). A community-based study from Texas found higher levels of HSV-1 antibodies in both blacks and Mexican-American adults, but no significant race/ethnic differences for EBV (Stowe et al., 2010). Recent national estimates identified higher levels of EBV antibodies in black children aged

Table 4
Linear regression of continuous logged Epstein–Barr Virus antibodies (AU/ml), Add Health Wave IV, weighted ($n = 11,050$).

	(1)	(2)	(3)	(4)	(5)
	β (SE)	β (SE)	β (SE)	β (SE)	β (SE)
Highest quartile lifetime stressful life events			0.010 (0.017)		
Highest quartile 12-month stressful life events				−0.009 (0.019)	
Cohen Perceived Stress Scale (ref = low)					
Medium					−0.011 (0.019)
High					−0.029 (0.020)
Male	−0.123** (0.013)	−0.124** (0.014)	−0.125** (0.014)	−0.124** (0.014)	−0.127** (0.014)
Completed education (ref = college/above)					
Less than high school		0.035 (0.032)	0.031 (0.033)	0.037 (0.032)	0.039 (0.032)
High school		0.012 (0.024)	0.010 (0.025)	0.013 (0.025)	0.015 (0.025)
Some college		0.013 (0.017)	0.011 (0.017)	0.013 (0.017)	0.015 (0.017)
Income (ref=>$87,000)					
<$35,000		0.009 (0.026)	0.008 (0.026)	0.010 (0.026)	0.015 (0.026)
$35,000–62,499		0.014 (0.022)	0.014 (0.022)	0.014 (0.022)	0.018 (0.022)
$62,500–87,499		−0.001 (0.020)	−0.001 (0.020)	−0.001 (0.020)	0.001 (0.020)
Race/ethnicity (ref = white)					
Black	0.139** (0.019)	0.136** (0.019)	0.134** (0.019)	0.137** (0.020)	0.136** (0.019)
Hispanic	0.026 (0.029)	0.024 (0.029)	0.024 (0.029)	0.025 (0.029)	0.024 (0.029)
Asian	−0.030 (0.032)	−0.025 (0.032)	−0.025 (0.032)	−0.026 (0.032)	−0.023 (0.032)
F-statistic	28.73	15.62	14.61	14.55	14.07

$**p < 0.01$, $*p < 0.05$, $+p < 0.10$.
Notes: Robust confidence intervals in parentheses; models also control for "other" race, missing income, recent infection, BMI, household size, and age. Coefficients represent % change in EBV antibodies associated with each category compared to reference group.

6–19 compared to white children, with no significant differences for Mexican-Americans (Ford and Stowe, 2013).

Our negative findings for stress and EBV are in contrast to the limited previous literature on associations between early-life stressors and later life markers of cell-mediated immune function in more specialized populations. Shirtcliff et al. identified higher levels of Herpes Simplex Virus Type 1 (HSV-1) antibody levels in adolescents who had been institutionalized (foreign orphanages) or physically abused in early childhood (Shirtcliff et al., 2009). McDade et al. and identified an association between traumatic life events and elevated EBV antibody levels for girls but not boys among 205 adolescents in the Great Smoky Mountains Study (McDade et al., 2000). Dowd et al. identified higher levels of CMV antibodies in children aged 6–17 in NHANES III for those with more extreme levels of disadvantage (below the poverty line), but no differences by family income above this threshold (Dowd et al., 2012). In the first study utilizing EBV data from Add Health, Slopen, et al. found an association between timing of childhood physical and sexual abuse and EBV antibody levels (Slopen et al., 2013a). It is possible that our index of stressful life events was a weaker predictor of EBV due to a broader range of severity compared to previous studies that focused exclusively on trauma or severe childhood experiences.

Our results suggest that race/ethnic differences in markers of immune function can emerge by early adulthood, prior to typical onset of chronic disease and age-related immune decline. Future work should test for potential explanations for the differences in EBV antibody levels between black and white young adults. Despite the lack of explanatory power of our measures of perceived stress and stressful life events, it is possible that other psychosocial exposures including discrimination could contribute to these differences. In a small longitudinal study of pregnant women in the U.S., black women had significantly higher EBV levels during pregnancy and postpartum compared to white women, and this difference was greatest for women reporting more experiences of discrimination (Christian et al., 2012). Given the higher levels of seropositivity of black youth at younger ages (Dowd et al., 2013), it is also possible that more frequent re-exposure to EBV could contribute to higher antibody levels.

Cell-mediated immune function, of which control over EBV is a component, plays an important role in eliminating viral infections, destroying bacteria and tumor cells, and defending against autoimmune diseases (Marshall, 2011). Stress-related immune alterations have been found to have associations with infectious illness, vaccine response, wound healing, as well as progression of cancer and other diseases of aging (Godbout and Glaser, 2006). Chronic or repeated EBV reactivation can increase the risk for lymphoid and epithelial malignancies, and has also been linked to autoimmune disorders including systemic lupus erythematosus, multiple sclerosis and rheumatoid arthritis. Despite these suggestive findings, the clinical implications of racial disparities in decreased cell-mediated immunity as measured by herpesvirus antibodies in the general and especially younger populations are not well established.

There are several limitations to this study. Despite the measurement of a comprehensive list of stressful life events, it is likely that the timing, duration, and severity of similar stressors varied across individuals, contributing to measurement error in our summary stress index that may have contributed to our null results for stress and EBV. Nonetheless, we saw similar null results for stressful events assessed in the last 12 months as well as perceived stress in the past two weeks, suggesting a consistent absence of stress-EBV associations in this sample. This dataset also only examined one indirect marker of immune function, antibody response to Epstein–Barr virus. It is possible that different immune markers may have showed stress-related associations in this sample. Previous studies have utilized a variety of different herpes viruses interchangeably to test stress and immune function associations, with little discussion of which markers are most useful or appropriate for such research (Glaser and Kiecolt-Glaser, 2005). Future work should refine the specific markers and populations for which such markers are likely to reveal useful variation and have health implications.

Despite these limitations, we found strong associations between SES, race/ethnicity and stressful life events in young adults, which may contribute to disparities in later chronic disease, whether through immune, neuroendocrine, or behavioral pathways (Seeman et al., 2010). Previous studies using Add Health identified links between stressful life events and smoking and depression (Adkins, 2009; Brown et al., 2007) and recent work identified significant associations between adverse relationship histories and self-reported health and depressive symptoms in this sample (Adam et al., 2011). This study also highlights that young black adults are more likely to have elevated EBV antibodies compared to their white peers, even adjusting for education and income. The long-term health implications and upstream determinants of these racial differences in immune function should be examined in future research.

Ethics statement

Use of the Add Health data was approved by the IRBs of Northwestern University and Stony Brook University, where all data analysis was conducted.

Acknowledgments

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