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The costs of high self-control in Black and Latino youth with asthma: Divergence of mental health and inflammatory profiles

Edith Chen[a,*], Madeleine U. Shalowitz[b], Rachel E. Story[c], Robin Hayen[a], Adam K.K. Leigh[a], Lauren C. Hoffer[a], Makeda K. Austin[a], Phoebe H. Lam[a], Gene H. Brody[d], Gregory E. Miller[a]

[a] Northwestern University, Institute for Policy Research & Department of Psychology, Evanston, IL, USA
[b] NorthShore University HealthSystem, Center for Clinical Research Informatics, Evanston, IL, USA
[c] NorthShore University HealthSystem, Department of Medicine, Evanston, IL, USA
[d] University of Georgia, Center for Family Research, Athens, GA, USA

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ABSTRACT

Emerging evidence in psychology suggests a paradox whereby high levels of self-control when striving for academic success among minority youth can have physical health costs. This study tested the skin-deep resilience hypothesis in asthma- whether minority youth who are striving hard to succeed academically experience good psychological outcomes but poor asthma outcomes. Youth physician-diagnosed with asthma (N = 276, M age = 12.99; 155 = White, 121 = Black/Latino) completed interviews about school stress and a self-control questionnaire. Outcomes included mental health (anxiety/depression) and ex-vivo immunologic processes relevant to asthma (lymphocyte Th-1 and Th-2 cytokine production, and sensitivity to glucocorticoid inhibition). Physician contacts were tracked over a one-year follow-up. For minority youth experiencing high levels of school stress, greater self-control was associated with fewer mental health symptoms (beta = −0.20, $p < .05$), but worse asthma inflammatory profiles (larger Th-1 and Th-2 cytokine responses, lower sensitivity to glucocorticoid inhibition), and more frequent physician contacts during the one-year follow-up (beta's ranging from 0.22 to 0.43, p's $< .05$). These patterns were not evident in White youth. In minority youth struggling with school, high levels of self-control are detrimental to asthma inflammatory profiles and clinical outcomes. This suggests the need for health monitoring to be incorporated into academic programs to ensure that 'overcoming the odds' does not lead to heightened health risks in minority youth.

1. Introduction

Recent research has documented a seemingly paradoxical effect whereby minority youth from low-income families who are exhibiting high levels of self-control and striving hard to succeed experience good mental health but are at greater risk for adverse physical health outcomes. In the mental health domain, low-income Black youth with higher levels of self-control report less depression, fewer delinquency problems, and less substance use, with similar patterns evident among Latino youth (Brody et al., 2013; Brody et al., 2016; Miller et al., 2016; Gaydosh et al., 2018; Chen et al., 2015). More generally, higher levels of self-control in childhood predict better grades in school, and in adulthood predict better life outcomes including a lower likelihood of using substances and of a criminal conviction, and higher income (Moffitt et al., 2011; Duckworth et al., 2012).

In contrast to these benefits, low-income Black youth with high levels of self-control have higher allostatic load scores (a multi-system indicator of chronic disease risk) (Brody et al., 2013) and faster epigenetic aging of their PBMCs (a metric based on DNA methylation reflecting the disparity between a person's biological and chronological ages) (Miller et al., 2015). They are also more likely to develop respiratory infections following a viral challenge (Miller et al., 2016) and to develop diabetes in young adulthood (Brody et al., 2016) compared to those from similar backgrounds but with low self-control. Similar health risks are evident in Latino youth with metabolic syndrome; however, no such risks are evident among White youth (Gaydosh et al., 2018; Miller et al., 2016). These patterns suggest that high self-control may actually be detrimental to physical health among youth who are members of underrepresented minority groups.

Why would this be? One explanation involves the "costs" that accrue to minority youth who attempt to overcome the adversities they face in life by working hard to succeed academically. Our theory is that

* Corresponding author at: Northwestern University, 2029 Sheridan Road, Evanston, IL 60208, USA.
E-mail address: edith.chen@northwestern.edu (E. Chen).

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a subset of minority youth see academic success as their pathway to a better life, and as a result they exhibit a hard-driving work ethic and determination to succeed that is reflected in high levels of self-control. However, for many of these students, the school experience remains a struggle for a number of reasons. Some of these students may be attending schools with limited resources that constrain their chances for academic success. Some of these students come from families that are limited in their availability or ability to provide academic support and resources to help their children succeed academically. And some of these minority students encounter school environments that are biased against them, in terms of beliefs about their racial/ethnic group's behaviors in school and academic potential. For the subset of minority youth who both experience these sorts of contextual school stresses and who nonetheless work to maintain the self-control needed to succeed academically (the combination of the two being important), this creates a unique set of experiences with health implications. Our theory postulates that high levels of self-control in the context of school struggles will produce benefits for many life outcomes, but at the same time will tax physiological systems and incur a physical health cost (Moffitt et al., 2011; Miller et al., 2015). That is, the ability to maintain high self-control and to persist with one's efforts despite a challenging school environment will lead to greater academic success, better jobs, and greater well-being as a result (relative to those who exhibit low self-control), but the effort involved in achieving these successes will take their toll in terms of physical health. Consistent with this scenario, low-income Black youth who make it to college are less likely to use substances compared with their peers who do not go to college; at the same time, they display higher allostatic load scores (Chen et al., 2015). Similarly, low-income Black youth who are high-striving are more likely to finish college and earn higher incomes as adults, but are at greater risk for adult diabetes than their low-striving peers (Brody et al., 2016). Low-income Latino youth who completed college showed less depression in adulthood but greater risk of metabolic syndrome compared with less-educated peers (Gaydosh et al., 2018). These diverging patterns were not evident in White youth (Gaydosh et al., 2018). These discrepancies between physical health and academic/mental health have been labeled 'skin-deep resilience,' to reflect the fact that these youth appear to be successful 'above the skin,' but biologically ('below the skin'), they are struggling (Brody et al., 2013).

Previous research has never tested whether these divergent patterns are evident in the context of a chronic disease such as asthma. In the present study, we investigated skin-deep resilience in a sample of youth with asthma, which allowed us to measure asthma-relevant immunologic processes. Asthma is a disease characterized by inflammation, constriction, and hypersensitivity of the airways. T-helper lymphocytes are key drivers of the pathology that initiates and maintains these processes. In response to asthma triggers, these cells assume functionally distinct phenotypes, and release two broad categories of cytokines: T-helper 1 (Th-1; which facilitate the elimination of intracellular pathogens like viruses) and T-helper 2 (Th-2; which facilitate the elimination of extra-cellular pathogens like helminth parasites). Excessive production of these cytokines is thought to be involved in multiple aspects of asthma-related pathology, including allergic sensitization, recruitment of eosinophils/neutrophils to the lungs, and downstream airway inflammation (Busse and Lemanske, 2001; Chung and Barnes, 1999; Spellberg and Edwards, 2001). Basic research initially pointed to a key role for Th-2 cytokines in asthma (Busse and Lemanske, 2001; Chung and Barnes, 1999). However, it should be noted that the Th-1/Th-2 distinction stems from mouse models of disease, and the distinction in humans is less clear, and has been criticized by some as simplistic and artificial (Gor et al., 2003; Mestas and Hughes, 2004). In fact, excessive production of both Th-1 and Th-2 cytokines are known to have roles in asthma pathogenesis and exacerbations (Holtzman et al., 2002).

Glucocorticoids play a major role in both the physiology and treatment of asthma. Physiologically, cortisol regulates a number of T-helper cell functions, and at higher concentrations it generally inhibits Th-1 and Th-2 cytokine production. These anti-inflammatory properties have made synthetic glucocorticoids a mainstay of asthma therapy. Nevertheless, there are marked individual variations in sensitivity to glucocorticoids (Busillo and Cidlowski, 2013), and a subset of patients display a pattern of steroid resistance, where these agents' anti-inflammatory properties are attenuated.

In addition to measuring the above immune processes, we also tested our theory's prediction that it is specifically in the context of struggling with school that high levels of self-control will incur its cost (because these youth see academic success as one of their few options for mobility). In this study, we measured chronic school stress using interview methods (the gold standard because it reduces subjective biases and errors found in self-reports; Monroe, 2008), as well as self-control in youth with asthma. We measured mental health (depression/anxiety) and asthma-relevant immune processes (cytokine production and glucocorticoid sensitivity) as outcomes during a lab visit, and physician contacts over a 1-year follow-up period. Our sample included Black, Latino, and White youth, and we stratified analyses by race, combining the Black and Latino youth into one group (based on the fact that previous studies found parallel patterns in these two groups, and that both are underrepresented minority groups that historically have experienced discrimination and disadvantage). Consistent with the skin-deep resilience theory, we hypothesized that among Black and Latino youth, there would be interaction effects between school stress and self-control predicting health. That is, minority youth who both experience high levels of stress in the school environment and who nonetheless persist with high self-control will experience better mental health but worse asthma profiles. We hypothesized that White youth would show no such divergent profiles.

2. Methods

2.1. Study participants

308 youth ages 9–17, physician-diagnosed with asthma, were recruited from Chicago and outlying suburbs/cities through one health care system, NorthShore University Health System, and one federally-qualified health center, Erie Family Health Center. Families were required to be fluent in English, and youth had to be free of acute respiratory illness at the time of the visit and have no other chronic physical illnesses. No children were on oral glucocorticoid medication. Youth gave written assent and parents provided written consent. This study was approved by the Northwestern, NorthShore, and Erie Institutional Review Boards. 155 of the sample was White, and 121 of the sample was Black or Latino- the remainder fell into smaller categories and were excluded from analyses, leaving a final sample size of 276.

2.2. Procedures

Participants came to our research center to complete interviews, questionnaires, and a blood draw. After the visit to the research center, parents were phoned every 3 months for a 1 year period to ask about physician contacts for asthma.

2.3. Measures

School stress. School stress was measured in youth using the UCLA Life Stress Interview (Hammen, 1991; Adrian & Hammen, 1993). This interview probes chronic strains within the school domain over the past 6 months, focusing on academic struggles, difficulty maintaining or variability in grades, the need for special supports/extra help academically, and behavioral and disciplinary troubles at school. Interviewers rated chronic school stress on a 1–5 scale, with higher numbers reflecting greater school strain. Interrater reliability across interviewers

was 0.93.

Self-control. Youth completed the 15-item Self-Control Inventory (Humphrey, 1982), which assesses constructs related to striving (persistence), the ability to stay focused on one's goals, the ability to plan ahead, and the ability to not get distracted from one's goals (e.g., 'How often do you work toward a goal?'). Items are scored on a 0–4 scale (ranging from 0 = never to 4 = almost always). Higher scores indicate higher levels of self-control (alpha = 79).

Immunologic measures-cytokine production. We measured Th-1 and Th-2 cytokine production by ex-vivo stimulated peripheral blood mononuclear cells (PBMCs). Although airway cells would better reflect activity at the site of disease, obtaining them requires an invasive procedure difficult for children without a clinical indication. Thus pediatric asthma studies often rely on PBMC-derived cytokines, which correlate with results obtained via bronchoalveolar lavage, and with eosinophil counts and disease severity (Corrigan and Kay, 1990; Gemou-Engesëth et al., 1994). 0.5×10^6 PBMCs were isolated by density-gradient centrifugation and incubated with 25 ng/mL of phorbol 12-myristate 13-acetate (PMA) + 1ug/mL of ionomycin (INO) for 24 h at 37 °C in 5% CO_2 (Rosenblum Lichtenstein et al., 2015; Chen et al., 2006; Chen et al., 2003). An unstimulated well was prepared with PBMCs but no mitogen to control for background cytokine levels. After incubation, supernatants were harvested and assayed in duplicate via electrochemiluminescence on a SECTOR Imager 2400A (Meso Scale Discovery, MSD) (Chowdhury et al., 2009). We used MSD's Human Th-1/Th-2 7-Plex Tissue Culture Kit, which measures both Th-2 (IL-4, IL-5, IL-10, and IL-13) and Th-1 (IFN-γ, IL-2) cytokines. Mean inter-assay coefficients of variation for duplicate pairs ranged from 1.50 to 3.64%. Values in the unstimulated wells were subtracted from those in the PMA/INO wells (to factor out background cytokine levels). Although the Th-1/Th-2 distinction has some limitations, we sought to address concerns about multiple outcome variables by using principal components analyses (PCA) to assess whether the number of cytokines could be reduced into factors that roughly corresponded to Th-1/Th-2 dimensions. These analyses were undertaken as part of a previous paper (Ehrlich et al., in press), and are briefly summarized here. Analyses revealed a 2-factor solution, in which cytokine loadings for the Th-2 factor (for the cytokines listed above) ranged from 0.87 to 0.97. This factor accounted for 68.1% of the variance. The Th-1 factor had cytokine loadings (for the cytokines listed above) ranging from 0.73 to 0.97, and accounted for 19.4% of the variance. Composite scores for Th-1 and Th-2 cytokines were derived by standardizing each cytokine and then averaging across standardized scores.

Glucocorticoid sensitivity. To measure sensitivity to glucocorticoid inhibition, the above protocol was repeated, this time with hydrocortisone added, and Th-1 and Th-2 cytokine production measured. 0.5×10^6 PBMCs were co-incubated with 25 ng/mL PMA, 1ug/mL INO, and 1.38×10^{-6} M hydrocortisone for 24 h at 37 °C in 5% CO_2, similar to previous studies (Miller et al., 2009; Miller & Chen, 2010). An unstimulated well (without PMA/INO or hydrocortisone) was also included. Supernatants were assayed using the MSD Th-1/Th-2 kit, and composite scores were created as described above. At the dose we used, cortisol suppresses production of Th-1/Th-2 cytokines, so higher values reflect greater insensitivity to glucocorticoid inhibition. However, we should note that because cytokines were aggregated into Th-1 and Th-2 composites, the mechanistic interpretation of our GC sensitivity metric is somewhat ambiguous, as higher values could reflect reduced PBMC sensitivity to the inhibitory effects of glucocorticoids or enhanced PBMC cytokine responses to the mitogen or both.

Physician contacts. Parents were contacted every 3 months for 1 year following the visit to the research center and asked about the number of times they had to contact their physician because of their child's asthma in the previous 3 months (not for planned visits or prescription refills, but rather because of asthma exacerbations). Frequency of physician contacts was summed across the 3, 6, 9, and 12 month phone calls.

Child anxiety/depression. Children completed the 13-item anxious/depressed scale from the validated Youth Self-Report (YSR) (Achenbach & Rescorla, 2003), focusing on the past 6 months (e.g., "I am nervous or tense" "I feel worthless or inferior"). Items are scored on a 0–2 scale (ranging from 0 = not true to 2 = very true or often true). Higher scores indicate more anxiety/depression symptoms (alpha = 0.84).

Covariates. Covariates included child gender; pubertal status (assessed via a validated self-report measure (Petersen et al., 1988))[1]; asthma severity (intrinsic intensity of disease, determined in patients with established asthma from the National Asthma Education and Prevention Program/Expert Panel Report 2 guidelines based on the higher of symptom frequency and medication use; Bacharier et al., 2004); and inhaled corticosteroid use and beta agonist use (number of days used in the past week).

2.4. Statistical analyses

In primary analyses, we conducted hierarchical multiple regression analyses according to the recommendations of Aiken and West (Aiken and West, 1991), in which asthma outcomes were predicted from three blocks of variables entered sequentially. The blocks were: (1) the covariates described above; (2) the main effects of school stress and self-control; and (3) the interaction between school stress and self-control. Separate models were fit for Black/Latino vs. White participants, consistent with previous research on skin-deep resilience that has conducted stratified analyses and documented effects within minority groups only (Gaydosh et al., 2018; Miller et al., 2016). This approach is also consistent with epidemiological approaches to dealing with race in analyses (e.g., Kershaw, 2015), and is one way to deal with concerns about different distributions of exposures across different groups of people (Oakes, 2006). Predictor variables were centered prior to analyses.

3. Results

3.1. Preliminary analyses

See Table 1 for information about the sample and the Online Supplement Table S1 for more details. Black/Latino youth had greater asthma severity ($t = 2.92$, $p = .004$), used beta agonists more often ($t = 2.46$, $p = .02$), produced greater amounts of Th-1 ($t = 2.13$, $p = .03$) and Th-2 cytokines following stimulation ($t = 2.00$, $p = .046$), had more frequent physician contacts ($t = 2.77$, $p = .01$), greater school stress ($t = 5.86$, $p < .001$), lower self-control ($t = 1.98$, $p = .049$), and were in more advanced pubertal stages ($t = 2.11$, $p = .04$). All analyses were conducted separately for Black/Latino participants and for White participants.

School stress and self-control were correlated at $r = -0.41$, $p < .001$. In terms of associations of covariates with outcomes, males had fewer anxiety/depression symptoms ($t = 4.24$, $p < .001$). Youth in more advanced pubertal stages had higher anxiety/depression scores ($r = 0.21$, $p < .001$). Youth age was not associated with any outcome. Youth with more severe asthma used inhaled corticosteroids ($r = 0.30$, $p < .001$) and beta agonists ($r = 0.24$, $p < .001$) more frequently, and had more frequent physician contacts ($r = 0.23$, $p < .001$). Youth who took inhaled corticosteroids more frequently had lower Th-2 cytokine production ($r = -0.14$, $p = .02$), and more frequent physician contacts ($r = 0.14$, $p = .01$). Beta agonist usage was not associated with outcomes.

See Online Supplement Tables S2 and S3 for more details.

[1] Analyses were re-run using age instead of pubertal status and patterns of results remained the same.

Table 1
Descriptive information about sample.

	Black/Latino (n = 121)			White (n = 155)		
	M	SD	%	M	SD	%
Gender – male			53			55
Child age	12.99	2.64		12.98	2.44	
Pubertal stage	3.40	1.09		3.11	1.17	
Beta agonist	1.83	2.39		1.20	1.86	
Inhaled corticosteroid	2.45	3.00		2.47	3.07	
Asthma severity	2.57	0.96		2.25	0.88	
School stress	2.22	1.01		1.63	0.67	
Self-control	39.15	7.30		40.92	6.79	
PMA/INO (Th-1)	0.14	0.96		−0.11	0.86	
PMA/INO (Th-2)	0.11	1.04		−0.13	0.82	
PMA/INO + Cortisol (Th-1)	0.10	0.99		−0.07	0.82	
PMA/INO + Cortisol (Th-2)	0.07	1.04		−0.08	0.80	
Physician contacts	1.40	1.65		0.85	1.59	
Anxiety/depression	6.41	5.16		6.72	4.53	

Note: Beta agonist and inhaled corticosteroid use refers to the number of days taken in the past week. Asthma severity ranges from 1 to 4. Pubertal stage ranges from 1 to 5. School stress ranges from 1 to 5. Self-control ranges from 0 to 60. Anxiety/depression ranges from 0 to 26. PMA/INO = phorbol myristate acetate/ionomycin. Cytokine production is represented by composite indicators derived from factor analyses. They include a Th-2 factor (IL-2, 4, 5, and 13) and a Th-1 factor (IFN-γ, IL-10). In all cases, values are corrected for non-specific production of each cytokine, then standardized and aggregated into composites.

3.2. Analyses with Black/Latino youth

See Tables 2 and 3 and Online Supplement Table S4 for details of analyses.

3.3. Immune outcomes

Th-2 cytokine production. Among minority youth, there were no main effects of either school stress or self-control on Th-2 cytokine production following PMA/INO stimulation. However, there was a significant interaction between school stress and self-control predicting Th-2

Table 2
Regression Analyses of School Stress and Self-Control Predicting Immunologic Outcomes among Black and Latino Youth.

	PMA/INO (Th-1)				PMA/INO (Th-2)			
	B	SE	95% CI	p	B	SE	95%CI	p
Step 1								
Gender	0.08	0.25	[−0.42, 0.57]	0.76	0.19	0.26	[−0.32, 0.70]	0.46
Pubertal stage	−0.05	0.12	[−0.28, 0.19]	0.70	0.03	0.12	[−0.21, 0.27]	0.81
Severity	−0.10	0.13	[−0.36, 0.15]	0.41	0.06	0.13	[−0.20, 0.32]	0.64
BA days	0.04	0.05	[−0.06, 0.14]	0.38	−0.04	0.05	[-0.14, 0.06]	0.44
ICS days	0.01	0.04	[−0.08, 0.09]	0.90	−0.03	0.04	[−0.11, 0.05]	0.48
	ΔR^2 = 0.02, p = .87				ΔR^2 = 0.03, p = .79			
Step 2								
School stress	−0.08	0.13	[−0.33, 0.17]	0.52	−0.01	0.13	[−0.27, 0.24]	0.92
Self-control	0.02	0.02	[−0.01, 0.05]	0.23	0.03	0.02	[-0.001, 0.07]	0.06
	ΔR^2 = 0.04, p = .22				ΔR^2 = 0.06, p = .10			
Step 3								
School stress × Self-control	0.03	0.01	[0.001, 0.06]	0.04	0.04	0.01	[0.02, 0.07]	0.002
	ΔR^2 = 0.05, p = .04				ΔR^2 = 0.10, p = .002			
	PMA/INO + Cortisol (Th−1)				PMA/INO + Cortisol (Th−2)			
	B	SE	95% CI	p	B	SE	95%CI	p
Step 1								
Gender	0.11	0.26	[−0.42, 0.63]	0.69	−0.12	0.27	[−0.66, 0.42]	0.65
Pubertal stage	−0.06	0.13	[−0.32, 0.21]	0.68	−0.06	0.13	[−0.33, 0.20]	0.63
Severity	−0.12	0.13	[−0.39, 0.14]	0.35	0.08	0.13	[−0.18, 0.35]	0.54
BA days	0.04	0.05	[−0.07, 0.14]	0.47	−0.05	0.05	[−0.16, 0.06]	0.34
ICS days	−0.02	0.04	[−0.10, 0.07]	0.66	−0.02	0.04	[−0.10, 0.07]	0.71
	ΔR^2 = 0.03, p = .85				ΔR^2 = 0.02, p = .93			
Step 2								
School stress	0.10	0.14	[−0.18, 0.38]	0.47	0.11	0.14	[−0.17, 0.39]	0.43
Self-control	−0.01	0.02	[−0.04, 0.03]	0.73	0.03	0.02	[−0.01, 0.06]	0.14
	ΔR^2 = 0.01, p = .59				ΔR^2 = 0.03, p = .33			
Step 3								
School stress × Self-control	0.024	0.015	[−0.01, 0.06]	0.13	0.05	0.02	[0.02, 0.08]	0.001
	ΔR^2 = 0.03, p = .13				ΔR^2 = 0.14, p = .001			

Note: PMA/INO = phorbol myristate acetate/ionomycin. BA = beta agonist. ICS = inhaled corticosteroid.

Table 3
Regression Analyses of School Stress and Self-Control Predicting Mental Health and Physician Contacts among Black and Latino Youth.

	Depression/Anxiety				Physician Contacts			
	B	SE	95% CI	p	B	SE	95%CI	p
Step 1								
Gender	−2.41	1.07	[−4.53, −0.29]	0.03	−0.55	0.34	[−1.23, 0.12]	0.11
Pubertal stage	1.05	0.52	[0.03, 2.07]	0.04	−0.15	0.17	[−0.48, 0.18]	0.38
Severity	0.19	0.55	[−0.90, 1.27]	0.73	0.39	0.18	[0.04, 0.74]	0.03
BA days	−0.12	0.21	[−0.54, 0.31]	0.59	0.05	0.07	[−0.08, 0.19]	0.43
ICS days	−0.14	0.18	[−0.49, 0.22]	0.44	0.00	0.06	[−0.12, 0.11]	0.95
		$\Delta R^2 = 0.17$, p = .003			$\Delta R^2 = 0.09$, p = .09			
Step 2								
School stress	0.19	0.49	[−0.78, 1.17]	0.70	0.11	0.18	[−0.24, 0.46]	0.54
Self-control	−0.25	0.07	[−0.38, −0.11]	< 0.001	0.02	0.02	[−0.03, 0.07]	0.40
		$\Delta R^2 = 0.13$, p < .001			$\Delta R^2 = 0.01$, p = .68			
Step 3								
School stress × Self-control	−0.13	0.06	[−0.24, −0.01]	0.03	0.04	0.02	[0.001, 0.08]	0.045
	$\Delta R^2 = 0.035$, p = .029				$\Delta R^2 = 0.04$, p = .045			

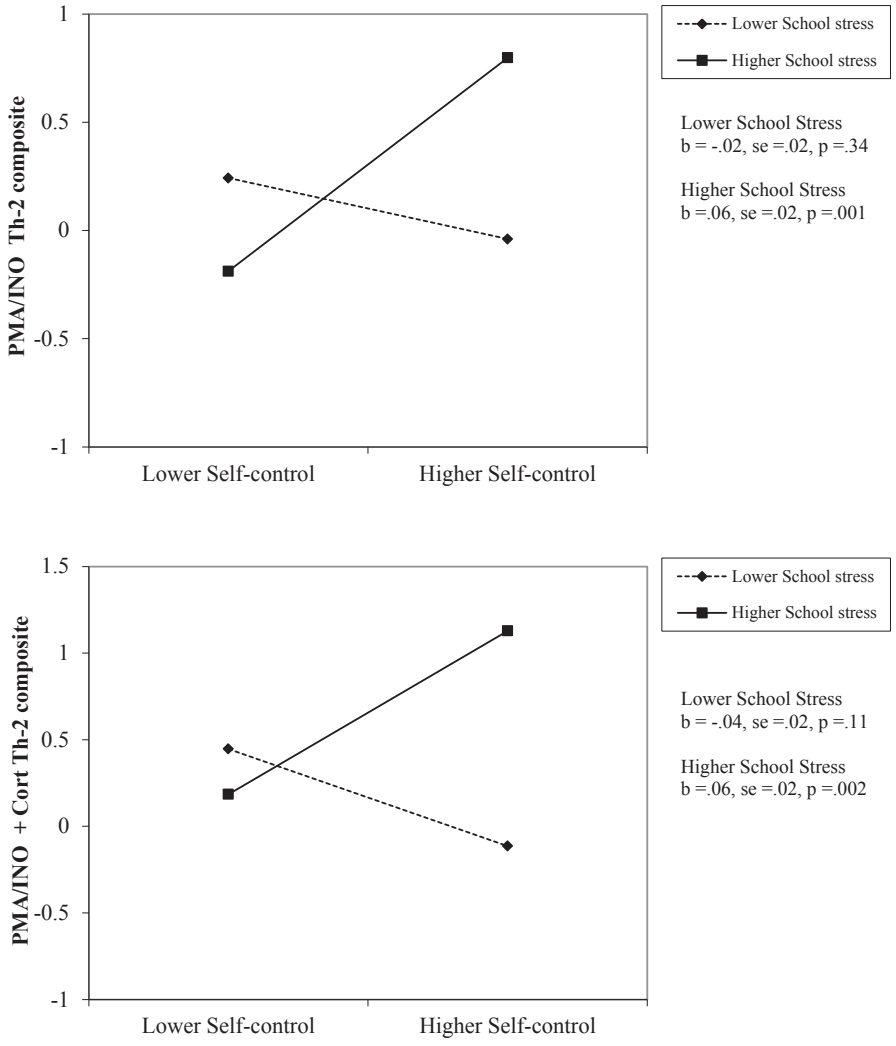

Fig. 1. Interaction between school stress and self-control predicting asthma immunologic outcomes in Black/Latino youth. Top panel depicts Th-2 cytokine responses following stimulation with PMA/INO. Bottom panel depicts glucocorticoid sensitivity, as indicated by Th-2 cytokine responses following stimulation with PMA/INO + cortisol (higher values indicate less glucocorticoid sensitivity). Cytokine composites represent values that have been standardized and averaged. The figure depicts estimated regression lines at ± 1 SD of school stress. Low and high self-control also refer to ± 1 SD.

cytokine responses (beta = 0.36, p = .002). See Fig. 1, top panel. At low levels of school stress, Th-2 cytokine responses do not vary by self-control (b = −0.02, se = 0.02, p = .34). However at higher levels of school stress, greater self-control is associated with larger amounts of Th-2 cytokine production (b = 0.06, se = 0.02, p = .001). Regions of significance testing indicated that the relationship between self-control and Th-2 cytokine production was significant above 0.19 SD of school stress.

Th-1 cytokine production. A similar pattern was evident for Th-1 cytokine production in minority youth: there were no main effects of either school stress or self-control, but a significant interaction emerged (beta = 0.25, p = .04). At low levels of school stress, Th-1 cytokine responses do not vary by self-control (b = −0.02, se = 0.02, p = .48). However at higher levels of school stress, greater self-control is associated with larger amounts of Th-1 cytokine production (b = 0.04, se = 0.02, p = .03). Regions of significance testing indicated that the relationship between self-control and Th-1 cytokine production was significant above 0.66 SD of school stress.

Glucocorticoid sensitivity: Th-2 cytokines. There were no main effects of either school stress or self-control among minority youth. However, there was a significant interaction (beta = 0.43, p = .001). Fig. 1, bottom panel, shows that at low levels of school stress, Th-2 cytokine responses do not vary by self-control (b = −0.04, se = 0.02, p = .11), whereas at higher levels of school stress, greater self-control is associated with less sensitivity to glucocorticoids' inhibitory properties (i.e., more Th-2 cytokine production despite the hydrocortisone, b = 0.06, se = 0.02, p = .002). Regions of significance testing indicated that the relationship between self-control and glucocorticoid sensitivity was significant above 0.40 SD of school stress. There were no significant effects for Th-1 cytokines.

3.4. Physician contacts

There were no main effects of either school stress or self-control in minority youth. Similar to the patterns for cytokine production, there was a significant interaction effect (beta = 0.22, p = .045). Fig. 2, top panel, shows that at low levels of school stress, physician contacts do not vary by self-control (b = −0.03, se = 0.03, p = .38), whereas at higher levels of school stress, greater self-control was associated with more frequent physician contacts (b = 0.05, se = 0.03, p = .06). Regions of significance testing indicated that the relationship between self-control and physician contacts was significant above 1.21 SD of school stress.[2]

3.5. Mental health

There was no main effect of school stress. There was a significant main effect of self-control (beta = −0.35, p < .001), such that greater self-control was associated with less anxiety/depression. There was also a significant interaction (beta = −0.20, p = .029). See Fig. 2, bottom panel. At low levels of school stress, anxiety/depression does not vary by self-control (b = −0.09, se = 0.10, p = .35), whereas at higher levels of school stress, greater self-control is associated with fewer anxiety/depression symptoms (b = −0.35, se = 0.08, p < .001). Regions of significance testing indicated that the relationship between self-control and anxiety/depression was significant above −0.49 SD of school stress.

3.6. Analyses with White participants

As predicted, among White youth, no evidence of skin-deep resilience emerged. No main effects of school stress emerged for any outcome. There was one main effect of self-control (beta = −0.27, p = .002), such that White youth with greater self-control had lower anxiety/depression. There were no interactions of school stress by self-control for any outcomes. See Online Supplement Tables S5 and S6 for details.

Supplementary analyses were conducted using multi-group path analyses to test whether the interaction coefficients significantly differed between the Black/Latino and White groups. Significant effects were found for anxiety/depression (Wald test = 4.90, p = .027) and marginally for Th-2 cytokine production following PMA/INO stimulation (Wald test = 3.51, p = .06). There were no significant effects for other outcomes.

4. Discussion

This study documents evidence of skin-deep resilience in minority youth with asthma specifically in the school context. Among Black and Latino youth with asthma who experienced high levels of school struggles, the greater their self-control, the better their mental health (fewer anxiety/depression symptoms) but the worse their asthma both immunologically (larger stimulated cytokine responses and lower glucocorticoid sensitivity) and clinically (more frequent physician contacts for asthma over a one-year follow-up period). White youth did not show divergent patterns of mental and physical health outcomes. These findings suggest one counterintuitive pathway to racial disparities in health: the idea that working hard in school to 'overcome the odds' may actually heighten health risks among minority youth with asthma.

These findings replicate a body of literature documenting skin-deep resilience in upwardly mobile Black and Latino youth, with previous research focused on health outcomes including allostatic load, epigenetic aging, and risks for diabetes, metabolic syndrome, and respiratory infection (Brody et al., 2013; Brody et al., 2016; Chen et al., 2015; Miller et al., 2016; Miller et al., 2015; Gaydosh et al., 2018). It also replicates previous research that has demonstrated that these patterns exist in minority youth/adults, but not in Whites (Gaydosh et al., 2018; Miller et al., 2016). The present study extends this work by demonstrating that the same phenomenon occurs with respect to childhood asthma among minority youth and by documenting links to disease-relevant immunologic processes.

The present study is also the first to directly measure school struggles and strain (using a gold standard interview method) when documenting skin-deep resilience. The use of an interview assessment allowed us to measure stress using an approach that reduces errors compared to self-report measures. The interactions support the theory that for minority youth, it is specifically in the context of struggles in the school environment (high levels of school stress) that high self-control produces a diverging profile of better mental health but worse physiologic profiles (Miller et al., 2015). This may be because for some minority youth, the school experience contains more formidable barriers to success. Many minority youth encounter structural discrimination, attend schools with limited resources, and experience competing demands between family and school. In addition, many minority youth have to work harder on their own to achieve academic successes, given that they are less likely to have parents who have attended college themselves (Aud et al., 2012). Many minority youth also encounter negative stereotypes about their racial/ethnic group's academic abilities, which can create anxiety and hinder academic performance (stereotype threat) (Steele, 2010). Minority youth are also more likely to be disciplined more severely by school personnel for similar infractions as White youth (Skiba et al., 2011). For minority youth who both have these types of experiences in the school setting and who nonetheless persist with high levels of self-control (the combination being important), this may result in persistent activation of their stress response systems (sympathetic nervous system, hypothalamic-pituitary-adrenal) that modulate T helper cell functions in a manner that exacerbates inflammation and constriction of the airways, and undermines asthma control (Miller et al., 2011; Gross and Levenson, 1997).

These study findings are broadly consistent with previous literature that has documented associations of other demographic variables, such as socioeconomic status, with cytokine production in asthma (Chen et al., 2003; Chen et al., 2006), and with studies that have shown associations of other psychological factors, such as stress and parental support, with cytokine production in asthma (Wright et al., 2010; Wright et al., 2004; Liu et al., 2002; Miller et al., 2009; Tobin et al.,

[2] Analyses were re-run using Poisson regression, and the interaction effect remained significant: b = 0.05, se = 0.02, p = .002.

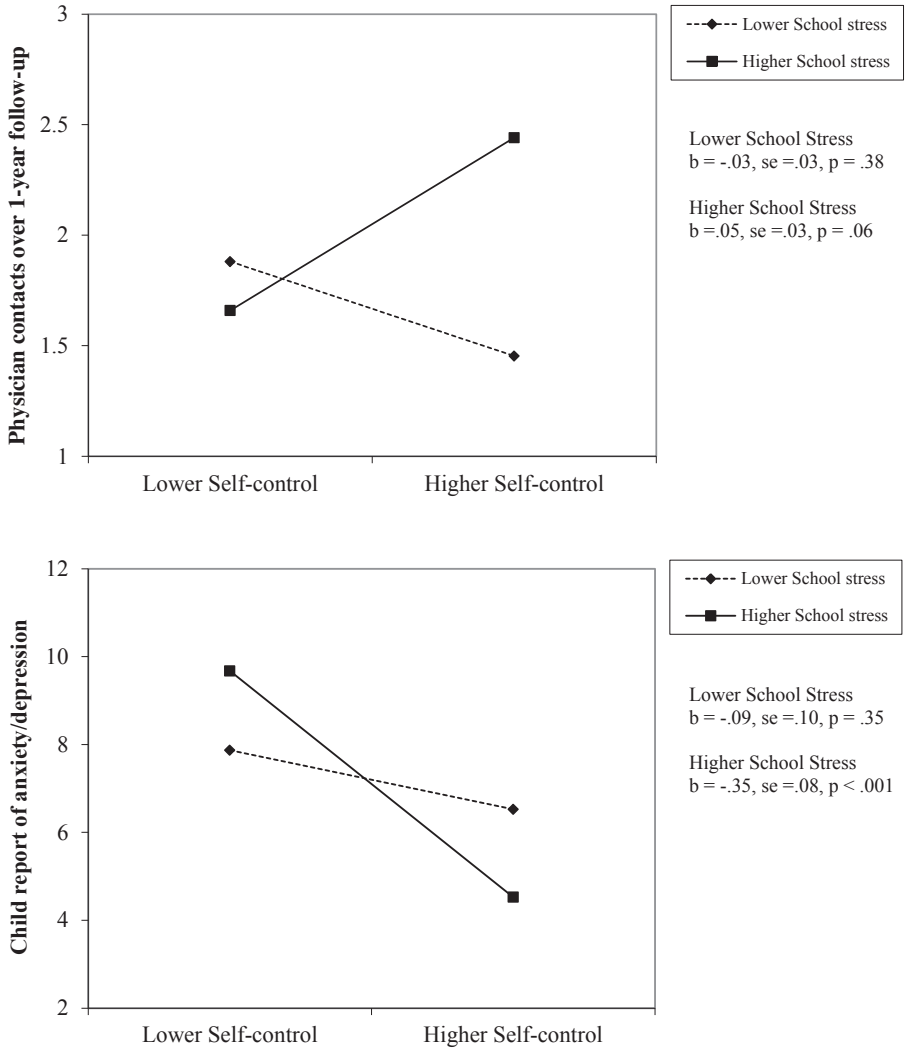

Fig. 2. Interaction between school stress and self-control predicting frequency of physician contacts and anxiety/depression in Black/Latino youth. Top panel depicts physician contacts during a one-year follow-up period. Bottom panel depicts anxiety/depression (higher scores indicate more anxiety/depression symptoms). The figure depicts estimated regression lines at ± 1 SD of school stress. Low and high self-control also refer to ± 1 SD.

2015). However, they extend previous research in documenting how demographic and psychological variables can interact to predict immunologic profiles in youth with asthma. In addition, the findings of greater cytokine production in minority youth compared to White youth are consistent with the epidemiologic pattern of minority youth having more frequent and severe asthma exacerbations and impairment (Gupta et al., 2006; Newacheck and Halfon, 2000).

We note that interaction effects were found for both Th-2 and Th-1 cytokine production, which is consistent with previous research (e.g., Marin et al., 2009) and with the idea that Th-1 and Th-2 processes can act in coordination with each other to contribute to asthma inflammation (Holtzman et al., 2002). Interaction effects were found for glucocorticoid sensitivity for Th-2, but not Th-1, cytokine production. The reasons for the lack of findings with Th-1 cytokines in the context of glucocorticoid inhibition is unclear. It is possible that a larger sample size would be needed to detect this effect; future studies should investigate the reliability and replicability of these patterns in larger samples.

Strengths of the present study include the focus on understanding predictors of health outcomes in minority populations; the mechanistic insights into links between psychological factors and a battery of immune processes relevant to asthma, including cytokine production and glucocorticoid sensitivity; the prospective nature of a one-year longitudinal follow-up assessing physician contacts; and the interview-based measure of school strain, a gold standard in life stress research (interviewer-rated stress assessments are considered more objective and less error-prone than participant self-reports because they rely on behavioral information and utilize interviewers to make standardized ratings). Limitations include the fact that causality cannot be determined from observational data, that the school interview was limited in its ability to assess contextual factors (e.g., school resources) and to discern the extent to which school struggles could be attributed to these factors, that a number of outcomes were measured cross-sectionally, and that very few parents (only 5 out of 276, across Whites/Blacks/Latinos) reported a hospitalization of their child over the one-year follow-up so we were unable to examine predictors of this outcome. In addition, it should be noted that the Th-1/Th-2 distinction, though utilized here to reduce the number of outcome variables, is simplistic and less clear-cut in humans (Mestas and Hughes, 2004; Gor et al., 2003). Lastly, we did not have the power to test a 3-way interaction (race × school stress × self-control) with this clinical sample. We note that although patterns emerged consistently in the Black/Latino group and not at all in the White group, the coefficients of the interaction terms were only sometimes significantly different from each other. This may have in part been due to inadequate power to test for coefficient differences in 2-way interaction effects in a diverse sample that

included Black, Latino, and White participants with asthma. Nonetheless, caution should be exercised in drawing conclusions about the different racial/ethnic groups differing from each other in their interaction patterns. In addition, we were not able to test for differences between Black and Latino youth or differences amongst different Latino groups, given the sample size. Future studies would benefit from recruiting larger clinical samples of color, as well as from including additional assessments of self-control (e.g., parent/teacher-report, behavioral measures of self-regulation), and longer-term follow-ups of mental health and asthma outcomes. Lastly, future studies should build upon the present study by testing psychosocial mediators of the stress × self-control interactions found here.

In sum, the present study found that among Black and Latino youth who are experiencing high levels of stress in their school environment, higher levels of self-control appear to be beneficial for mental health, but are detrimental for immunologic processes relevant to asthma and physician contacts for asthma. These findings suggest that psychological traits that have typically been considered positive, such as self-control, may actually serve as a 'double-edged sword' for certain minority youth, with both positive and negative consequences. As such, these findings are important for encouraging a focus on physical health/biological profiles in academic programs that promote constructs such as self-regulation, grit, and persistence, particularly among minority youth, so that 'overcoming the odds' does not lead to heightened health risks. Among these youth, interventions that combine promoting academic success with health education and regular health monitoring may be important for the ultimate goal of preventing and treating asthma in youth who are otherwise on a track to successful life outcomes.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.bbi.2019.02.031.

References

Achenbach, T.M., Rescorla, L.A., 2003. Manual for the ASEBA adult forms and profiles. University of Vermont, Research Center for Children, Youth, and Families, Burlington, VT.

Adrian, C., Hammen, C., 1993. Stress exposure and stress generation in children of depressed mothers. Retrieved from ISI:A1993KW45900022.. J. Consult. Clin. Psychol. 61 (2), 354–359.

Aiken, L.S., West, S.G., 1991. Multiple Regression: Testing and Interpreting Interactions. Sage Publications, London.

Aud, S., Hussar, W., Johnson, F., Kena, G., Roth, E., Manning, E., Zhang, J., 2012. The Condition of Education, 2012 (NCES 2012–045). U.S. Department of Education, National Center for Education Statistics, Washington DC.

Bacharier, L.B., Strunk, R.C., Mauger, D., White, D., Lemanske, R.F., Sorkness, C.A., 2004. Classifying asthma severity in children: Mismatch between symptoms, medication use, and lung function. Retrieved from ISI:000223217300017.. Am. J. Respir. Crit. Care Med. 170 (4), 426–432.

Brody, G.H., Yu, T., Chen, E., Miller, G.E., Kogan, S.M., Beach, S.R.H., 2013. Is resilience only skin deep? Rural African Americans' preadolescent socioeconomic status-related risk and competence and age 19 psychological adjustment and allostatic load. Psychol. Sci. 24, 1285–1293.

Brody, G.H., Yu, T., Miller, G.E., Chen, E., 2016. Resilience in adolescence, health, and psychosocial outcomes. Pediatrics 138, e20161042.

Busillo, J.M., Cidlowski, J.A., 2013. The five Rs of glucocorticoid action during inflammation: ready, reinforce, repress, resolve, and restore. Trends Endocrinol. Metab. 24 (3), 109–119. https://doi.org/10.1016/j.tem.2012.11.005.

Busse, W.W., Lemanske, R.F., 2001. Advances in immunology: Asthma. N. Engl. J. Med. 344 (5), 350–362.

Chen, E., Miller, G.E., Brody, G.H., Lei, M., 2015. Neighborhood poverty, college attendance, and diverging profiles of substance use and allostatic load in rural African American youth. Clin. Psychol. Sci. 3 (5), 675–685. https://doi.org/10.1177/2167702614546639.

Chen, E., Fisher Jr., E.B., Bacharier, L.B., Strunk, R.C., 2003. Socioeconomic status, stress, and immune markers in adolescents with asthma. Psychosom. Med. 65, 984–992.

Chen, E., Hanson, M.D., Paterson, L.Q., Griffin, M.J., Walker, H.A., Miller, G.E., 2006. Socioeconomic status and inflammatory processes in childhood asthma: The role of psychological stress. Retrieved from ISI:000237436300007.. J. Allergy Clin. Immunol. 117 (5), 1014–1020.

Chowdhury, F., Williams, A., Johnson, P., 2009. Validation and comparison of two multiplex technologies, luminex and mesoscale discovery, for human cytokine profiling. J Immunol Meth. 340 (1), 55–64. https://doi.org/10.1016/j.jim.2008.10.002.

Chung, K.F., Barnes, P.J., 1999. Cytokines in asthma. Thorax 54, 825–857.

Corrigan, C.J., Kay, A.B., 1990. CD4 T-lymphocyte activation in acute severe asthma: relationship to disease severity and atopic status. Am. Rev. Respir. Dis. 141, 970–977.

Duckworth, A.L., Quinn, P.D., Tsukayama, E., 2012. What No Child Left Behind leaves behind: the roles of IQ and self-control in predicting standardized achievement test scores and report card grades. J. Educ. Psychol. 104, 439–451.

Ehrlich, K.B., Miller, G.E., Shalowitz, M., Story, R., Levine, C., Williams, D., et al., in press. Secure base representations in children with asthma: Links with symptoms, family asthma management, and cytokine regulation. Child Develop.

Gaydosh, L., Schorpp, K., Chen, E., Miller, G., Harris, K.M., 2018. College completion predicts lower depression but higher metabolic syndrome among disadvantaged minorities in young adulthood. Proc. Natl. Acad. Sci. 115, 109–114.

Gemou-Engesëth, V., Kay, A.B., Bush, A., Corrigan, C.J., 1994. Activated peripheral blood CD4 and CD8 T-lymphocytes in child asthma: correlation with eosinophilia and disease severity. Pediatr. Allergy Immunol. 5, 170–177.

Gor, D.O., Rose, N.R., Greenspan, N.S., 2003. Th1-Th2: a Procrustean paradigm. Nat. Immunol. 4, 503–505.

Gross, J.J., Levenson, R.W., 1997. Hiding feelings: the acute effects of inhibiting negative and positive emotion. J. Abnorm. Psychol. 106 (1), 95–103.

Gupta, R.S., Carrion-Carire, V., Weiss, K.B., 2006. The widening black/white gap in asthma hospitalizations and mortality. Retrieved from ISI:000235687300018. J. Allergy Clin. Immunol. 117 (2), 351–358.

Hammen, C., 1991. Generation of stress in the course of unipolar depression. J. Abnorm. Psychol. 100, 555–561.

Holtzman, M.J., Morton, J.D., Shornick, L.P., Tyner, J.W., O'Sullivan, M.P., Antao, A., Walter, M.J., 2002. Immunity, inflammation, and remodeling in the airway epithelial barrier: epithelial-viral-allergic paradigm. Retrieved from ISI:000173028700002. Physiol. Rev. 82 (1), 19–46.

Humphrey, L.L., 1982. Children's and teacher's perspectives on children's self-control: the development of two rating scales. J. Consult. Clin. Psychol. 50, 624–633.

Kershaw, K.N., Osypuk, T.L., Do, D.P., De Chavez, P.J., Diez Roux, A.V., 2015. Neighborhood-level racial/ethnic residential segregation and incident cardiovascular disease. Circulation 131, 141–148.

Liu, L.Y., Coe, C.L., Swenson, C.A., Kelly, E.A., Kita, H., Busse, W.W., 2002. School examinations enhance airway inflammation to antigen challenge. Am. J. Respir. Crit. Care Med. 165, 1062–1067.

Marin, T.J., Chen, E., Munch, J.A., Miller, G.E., 2009. Double-exposure to acute stress and chronic family stress is associated with immune changes in children with asthma. Psychosom. Med. 71 (4), 378–384. https://doi.org/10.1097/PSY.0b013e318199dbc3.

Mestas, J., Hughes, C.C., 2004. Of mice and not men: differences between mouse and human immunology. Retrieved from. J. Immunol. 172 (5), 2731–2738. http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=14978070.

Miller, G.E., Cohen, S., Janicki-Deverts, D., Brody, G.H., Chen, E., 2016. Viral challenge reveals further evidence of skin-deep resilience in African Americans from disadvantaged backgrounds. Health Psychol. 35, 1225–1234.

Miller, G.E., Chen, E., 2010. Harsh family climate in early life presages the emergence of a proinflammatory phenotype in adolescence. Psychol Sci 21 (6), 848–856. https://doi.org/10.1177/0956797610370161.

Miller, G.E., Chen, E., Parker, K.J., 2011. Psychological stress in childhood and susceptibility to the chronic diseases of aging: moving toward a model of behavioral and biological mechanisms. Psychol Bull 137 (6), 959–997. https://doi.org/10.1037/a0024768.

Miller, G.E., Gaudin, A., Zysk, E., Chen, E., 2009. Parental support and cytokine activity in childhood asthma: the role of glucocorticoid sensitivity. J. Allergy Clin. Immunol. 128 (5), 970–976. https://doi.org/10.1016/j.jaci.2008.12.019.

Miller, G.E., Yu, T., Chen, E., Brody, G.H., 2015. Self-control forecasts better psychosocial outcomes but faster epigenetic aging in low-SES youth. Proc. Natl. Acad. Sci. U.S.A. 112 (33), 10325–10330. https://doi.org/10.1073/pnas.1505063112.

Moffitt, T.E., Arseneault, L., Belsky, D., Dickson, N., Hancox, R.J., Harrington, H., Caspi, A., 2011. A gradient of childhood self-control predicts health, wealth, and public safety. Proc. Natl. Acad. Sci. U.S.A. 108 (7), 2693–2698. https://doi.org/10.1073/pnas.1010076108.

Monroe, S.M., 2008. Modern approaches to conceptualizing and measuring human life stress. Ann. Rev. Clin. Psychol. 4, 33–52.

Newacheck, P.W., Halfon, N., 2000. Prevalence, impact, and trends in childhood disability due to asthma. Archiv. Pediatr. Adoles. Med. 154, 287–293.

Oakes, J.M., 2006. Advancing neighborhood effects research: selection, inferential support, and structural confounding. Int. J. Epidemiol. 35, 643–647.

Petersen, A.C., Crockett, L., Richards, M., Boxer, A., 1988. A self-report measure of pubertal status: reliability, validity, and initial norms. J. Youth Adolesc. 17, 117–133.

Rosenblum Lichtenstein, J.H., Hsu, Y.H., Gavin, I.M., Donaghey, T.C., Molina, R.M., Thompson, K.J., Brain, J.D., 2015. Environmental mold and mycotoxin exposures elicit specific cytokine and chemokine responses. PLoS One 10 (5), e0126926. https://doi.org/10.1371/journal.pone.0126926.

Skiba, R.J., Horner, R.H., Chung, C.G., Rausch, M.K., May, S.L., Tobin, T., 2011. Race is not neutral: a national investigation of African American and Latino

disproportionality in school discipline. School Psychol. Rev. 40, 85–107.
Spellberg, B., Edwards, J.E., 2001. Type 1 type 2 immunity in infectious diseases. Retrieved from ISI:000166012300012.. Clin. Infect. Dis. 32 (1), 76–102.
Steele, C., 2010. Whistling Vivaldi: And Other Clues to how Stereotypes Affect Us. W.W. Norton and Company, New York, NY.
Tobin, E.T., Kane, H.S., Saleh, D.J., Wildman, D.E., Breen, E.C., Secord, E., Slatcher, R.B., 2015. Asthma-related immune responses in youth with asthma: associations with maternal responsiveness and expressions of positive and negative affect in daily life. Psychosom. Med. 77 (8), 892–902. https://doi.org/10.1097/PSY.0000000000000236.
Wright, R.J., Visness, C.M., Calatroni, A., Grayson, M.H., Gold, D.R., Sandel, M.T., Gern, J.E., 2010. Prenatal maternal stress and cord blood innate and adaptive cytokine responses in an inner-city cohort. Am. J. Respir. Crit. Care Med. 182 (1), 25–33. https://doi.org/10.1164/rccm.200904-0637OC.
Wright, R.J., Finn, P., Contreras, J.P., Cohen, S., Wright, R.O., Staudenmayer, J., Gold, D.R., 2004. Chronic caregiver stress and IgE expression, allergen-induced proliferation, and cytokine profiles in a birth cohort predisposed to atopy. J. Allergy Clin. Immunol. 113 (6), 1051–1057.