HHS Public Access

Author manuscript

Obesity (Silver Spring). Author manuscript; available in PMC 2016 June 08.

Published in final edited form as:

Obesity (Silver Spring). 2016 May ; 24(5): 1148–1153. doi:10.1002/oby.21462.

Prepubertal Children Exposed to Concentrated Disadvantage: An Exploratory Analysis of Inflammation and Metabolic Dysfunction

Maura Kepper[1], **Melinda Sothern**[1,2,4], **Jovanny Zabaleta**[1,2,3], **Eric Ravussin**[4], **Cruz Velasco-Gonzalez**[5], **Claudia Leonardi**[6], **Lauren Griffiths**[1], **Chi Park**[6], **John Estrada**[2,3], and **Richard Scribner**[6]

[1]School of Public Health, Behavioral & Community Health Sciences Department, Louisiana State University Health Sciences Center, New Orleans, Louisiana, USA

[2]School of Medicine, Department of Pediatrics, Louisiana State University Health Sciences Center, New Orleans, Louisiana, USA

[3]Stanley S. Scott Cancer Center, Louisiana State University Health Sciences Center, New Orleans, Louisiana, USA

[4]Pennington Biomedical Research Center, Baton Rouge, Louisiana, USA

[5]School of Public Health, Department of Biostatistics, Louisiana State University Health Sciences Center, New Orleans, Louisiana, USA

[6]School of Public Health, Department of Epidemiology, Louisiana State University Health Sciences Center, New Orleans, Louisiana, USA

Abstract

Objective—It is unclear whether physiologic and metabolic biomarkers are associated with chronic stressors evidenced during early childhood.

Methods—Cross-sectional data were obtained from a cohort of healthy, prepubertal (Tanner stage <2) children (n = 96; age: 8.06 [7.8] years; M = 51 [53%]; F = 45 [47%]; African-American = 26 [27%]; Caucasian = 70 [73%]; with obesity = 21 [22%]; without obesity = 75 [78%]) from the MET study. Body mass index z-score (z_BMI), total body fat (BF), visceral adipose tissue (VAT), intrahepatic and intramyocellular lipids, and insulin resistance (HOMA-IR) were measured. Chronic stress was assessed using neighborhood concentrated disadvantage index (CDI) for the U.S. Census tracts in which participants resided. Spearman's rank correlations were used to examine relationships, accounting for sex and race.

Results—CDI was not positively associated with inflammatory and metabolic markers of dysfunction. However, z_BMI (−0.234, P = 0.023), BF (−0.228, P = 0.028, n = 95), and VAT (−0.241, P = 0.042, n = 74) were significantly negatively associated with CDI. When stratifying by race, these relationships remained significant in Caucasian children only.

Correspondence: Maura Kepper (; Email: mmohle@lsuhsc.edu)

Disclosure: The authors declare no conflict of interest.

Conclusions—These findings suggest chronic stress during early childhood is not associated with inflammatory and metabolic biomarkers, typically observed in adults. Therefore, exposure to stress during this critical developmental period may remain latent and emerge during a later developmental stage.

Introduction

Understanding the complex interactions of how the environment "gets under the skin" to predispose the states of metabolic dysfunction associated with obesity, diabetes, cardiovascular disease, and cancer requires a developmental perspective. Research that acknowledges the role of the environment during critical stages in the life course is limited (1-3). The developmental origins perspective proposes that there are critical developmental periods characterized by plasticity in genomic expression that can be affected by environmental conditions that ultimately define an adult phenotype associated with a variety of chronic diseases (4-8). The prenatal and perinatal periods as well as childhood and early adolescence have all been recognized as critical developmental periods in the life course. It has been shown that during critical periods of development, environmental conditions act through epigenetic mechanisms to affect the expression of genes involved in physiologic pathways that attempt to maintain biologic homeostasis given the environmental conditions an organism finds itself in (9-11).

There are two physiologic pathways where variability in the expression of particular genes could lead to physiologic and metabolic dysfunction associated with several adult chronic disease states. These pathways are the hypothalamic pituitary adrenal (HPA) pathway and the sympathetic adrenal medullary (SAM) pathway (2). There is growing recognition that social or nutritive stress represent the environmental exposures that initiate the developmental changes in these inflammatory pathways (8,12,13). It has been shown in both animal and human studies that social and nutritive stress affect the expression of critical genes involved in the HPA and SAM pathways (e.g., gluccocorticoid receptor) (8). The result is a pro-inflammatory adult phenotype evidenced by physiologic (e.g., visceral adiposity) and metabolic dysfunction (e.g., impaired insulin sensitivity) as well as elevated levels of a number of inflammatory cytokines, such as interleukin (IL)-6 and tumor necrosis factor (TNF)-α. Sustained metabolic and physiologic dysfunction (e.g., metabolic syndrome) is associated with a variety of negative health outcomes including cardiovascular disease, type 2 diabetes, and certain cancers (14). However, identifying the time period when exposures occur, as well as the temporal sequencing of exposure to the emergence of elevated inflammation and metabolic dysfunction, is a critical component of the developmental origins perspective that has not been clearly elucidated.

While there have been a number of literature reviews documenting the relationship between early life stress and adult disease, few studies have attempted to characterize the timing of exposure to stress throughout the life course and the emergence of the metabolic and physiologic changes associated with the metabolic syndrome (1,3,8,12,15). Some studies have suggested exposure to stressors during the critical developmental stages is evidenced by physiologic and or metabolic changes in childhood. For example, Gillman et al. (2008) found that prenatal and perinatal stressors (e.g., smoking, breast feeding duration) were

associated with obesity at 3 years old (16). However, they did not distinguish between visceral and subcutaneous obesity or assess any markers of metabolic dysfunction that might indicate alterations in gene expression. Another study of prepubertal, Hispanic children (Tanner stage < 3) had mixed results (17). Only school stress was associated with increased visceral adiposity and cortisol awakening response while total stress and other measured stressors were not (17). However, several studies have implied childhood and early adolescence may be a protected period where the effects of early stressors on gene expression are dormant. For example, Hankin et al. (2010) followed depressed and normal children through adolescence (preschool to ninth grade) and found that compared with normal children depressed children had hyporeactive cortisol responses as children but not during adolescence (18). Neurobiologists believe that childhood is a protected stage with regard to metabolic and physiologic responses to stress, a stage that ends with the onset of puberty (12). Consequently, the physiologic and metabolic changes associated with chronic exposure to social and nutritive stress in adults may not be evidenced in children exposed to the same stressors until after puberty.

Identifying the stage of maturation in which the physiologic mechanisms are reset and then sustained to adapt to a stressful environment will be essential to understanding the developmental origins of health outcomes, particularly metabolic and inflammatory profiles (10). The purpose of this study is to begin to characterize the emergence of the pro-inflammatory phenotype associated with the social stress of living in an environment characterized by concentrated disadvantage. This exploratory, cross-sectional study assesses the metabolic and inflammatory biomarkers in prepubertal children (Tanner stage <2) and determines whether there is an association between neighborhood disadvantage concentrated disadvantage index, CDI and these biomarkers. This is one of the first articles to document these relationships in an exclusively prepubertal, white and black cohort of healthy children with and without obesity using state-of-the-art measures of adiposity and metabolic health.

Methods

Study population

Children in the MET (Mechanisms for the Metabolic Syndrome in Pre-pubertal Youth) study were accessed to assess this effect. The characteristics of the children have been described previously (19,20). In short, exclusively prepubertal, healthy children with and without obesity ages 7–9 years were enrolled from October 2005 through December 2010. The original study included black, white, Asian, Pacific Islander, and Hispanic youth; however, only black and white children were included for this analysis as only one Pacific Islander and one Hispanic child were enrolled. Phone interviews with the parent/guardians pre-enrolled participants before final eligibility was determined by a complete medical examination by a pediatrician and screening blood test that included a comprehensive metabolic panel, a complete blood count, and a Tanner staging examination to confirm prepubertal status (21). Exclusion criteria included Tanner >2, cardiovascular disease or liver disease, being born from a mother with gestational diabetes, and/or immediate family history of type 1 or type 2 diabetes. Parent/guardians provided informed consent and the participants gave written assent prior to enrollment. The study was approved by the

institutional review boards at the Louisiana State University Health Sciences Center and Children's Hospital in New Orleans, LA and Woman's Hospital and the Pennington Biomedical Research Center in Baton Rouge, LA.

Anthropometrics and metabolic parameters

Anthropometric measurements were determined as previously described (19,20). Briefly, body mass index (BMI) was determined by the ratio weight (kg)/height (m^2), and this was used to obtain the BMI z-score (z_BMI), based on age, gender, and race along with other criteria (22). Insulin resistance (HOMA-IR) was estimated by the homeostasis model assessment based on previously published methods (23); visceral adipose tissue (VAT) and subcutaneous adipose tissue (SAT) were determined by magnetic resonance imaging (MRI) in the fourth through fifth lumbar vertebrae area. A trained technician acquired spinecho T1 weighted (TR ¼ 500; TE ¼ 20) images. The manual trackball technique was used to define adipose tissue. The MRI fat signal between the skin and abdominal muscle walls and intra-abdominal adipose tissue area, along with signals from intraperitoneal, mesenteric, and omental depots, was used to calculate SAT as suggested previously (23-25). Total body fat (BF) was measured by dual-energy X-ray absorptiometry. Intrahepatic lipids (IHL) and intramyocellular lipids (IMCL) were assessed by proton magnetic resonance spectroscopy as detailed previously (20).

Circulating levels of pro- and anti-inflammatory molecules

Fasting serum levels (pg ml^{-1}) of IL-1b, IL-6, IL-8, TNF-α, and MCP-1 and adiponectin were measured using Milliplex Map Kit (Millipore Corporation, Billerica, MA), as recommended by the manufacturer. Briefly, 25 ml of a 1:100 dilution of serum was mixed with immunobeads (supplied in the kit) and incubated overnight at 4°C, washed twice with a buffer to remove unbound products, and incubated with a detection antibody for 1 h at room temperature (20–25°C) with agitation. Finally, streptavidin-phycoerythrin was added and the samples were incubated 30 min at room temperature and washed twice and the fluorescence was detected on a BioPlex system (Bio-Rad, Hercules, CA). The unknown samples (sera) were analyzed in duplicate using a standard curve of known concentrations of each one of the tested molecules. The run included negative and control samples. To visualize the correlations, scatterplots of pairs of markers with significant Spearman's correlation were constructed using the logarithmic values of the TNF-α, IHL, and IL-8 measurements. Owing to limits in the availability of these pediatric participant samples obtained from an ancillary study (26), we were unable to confirm the results by enzyme-linked immunosorbent assay, but our experience shows a strong correlation between the two techniques (Milliplex and enzyme-linked immunosorbent assay) (27).

Concentrated disadvantage index

Concentrated disadvantage is a widely used, area based index of social deprivation (28). The method for generating CDI is described in detail in the PhenX Toolkit, a collaboration between the Research Triangle Institute and the National Human Genome Research Institute to develop consensus measures for phenotypes and exposures (29). CDI is one of the most important indicators for a host of individual outcome measures that are incorporated at the neighborhood (i.e., census tract) level (30). The index is generated from a factor analysis of

the following census tract data extracted from the 2000 U.S. Census (during the study participants' prepubertal years): percent of individuals below the poverty line, percent of individuals on public assistance, percent female-headed households, percent unemployed, percent less than age 18, and percent black. Study participants were geo-coded and linked to their census tract data. The factor analysis (principal component analysis using varimax rotation methods) confirmed the emergence of a single factor of concentrated disadvantage thereby undermining the likelihood of unique effects for any of the component variables.

Statistical analysis

Statistical analyses were carried out in SAS 9.3 (SAS Institute, Cary, NC). Tests were conducted at 0.05 significance level. For each analysis, effective sample sizes are reported as data are not available for all patients on all measured variables, as previously explained (19,20). Although the nature of the data set is multilevel, no multilevel analysis was implemented because 79.2% of census tracts included only one participant. Therefore, Spearman's rank correlations accounting for sex and race were used to examine the overall relationships between CDI and the following metabolic and inflammatory markers: z_BMI, BF, VAT, SAT, HOMA-IR, IMCL, IHL, IL-6, IL-8, and TNF-α. Furthermore, Spearman's rank correlations accounting for sex were used across and within races to examine the relationships between each individual CDI factor (percent of individuals below the poverty line, percent of individuals on public assistance, percent female-headed households, percent unemployed, percent less than age 18 years, and percent black) and each inflammatory and metabolic marker.

Results

Demographic, anthropometric, and CDI data were available for 96 black and white children in the original MET study; inflammatory and metabolic markers were available in a subgroup of 40 of these children. Analyses were carried out on the most complete data (Tables 1-3). The study participants were 53% male and had a mean (SD) age of 8.06 (0.78) years (Table 1). As reported previously, there were no significant differences in inflammatory and metabolic markers between white and black children, except for HOMA-IR (31). Black children in the study had higher levels of insulin resistance than the white children (Table 1).

Several associations between neighborhood CDI and the inflammatory and metabolic markers were noted. With regard to the metabolic markers, we observed a negative association between CDI and three metabolic parameters: z_BMI ($P = 0.023$), BF ($P = 0.028$), and VAT ($P = 0.042$) (Table 2). When stratified by race, these relationships only remained significant in white children (respectively, $P = 0.025$, $P = 0.015$, and $P = 0.035$). No significant relationships were found between CDI and inflammatory markers (e.g., IL-6, IL-8, TNF-α). However, a negative relationship between IL8 and CDI ($P = 0.201$), particularly in black children ($P = 0.124$), approached significance. Further investigation of this potential relationship is warranted in a larger population.

We next examined the correlation between each inflammatory and metabolic marker and each CDI factor (i.e., percent of individuals below the poverty line, percent of individuals on

public assistance, percent female-headed households, percent unemployed, percent less than age 18 years, and percent black) in order to determine whether the inclusion of percent black in the index represented a potential bias to the observed associations between CDI and inflammatory and metabolic markers. As can be observed in Table 3, individually, percent female-headed household was negatively related to z_BMI (P=0.011), BF (P = 0.008), VAT (P = 0.003), and SAT (P = 0.005). Additionally, percent unemployed was negatively related to BF (P =0.047) and percent less than age 18 years positively related to VAT (P = 0.038). When stratified by race and partialed for sex, percent female-headed household only remained inversely related to z_BMI (P = 0.008), BF (P = 0.003), VAT (P = 0.002), and SAT (P = 0.002), in white children.

Discussion

The results indicate that, in contrast to adults, neighborhood disadvantage was not positively associated with markers of inflammation and metabolic dysfunction in prepubertal children in this sample. Conversely, there was an unexpected negative relationship between neighborhood disadvantage and obesity and early markers of metabolic disease in these prepubertal children. Assuming the levels of concentrated disadvantage were sufficient to stimulate a stress response in these children, the findings support the neurobiological argument that early childhood represents a protected period when the effects of social and or nutritive stress are not evidenced by a pro-inflammatory state or metabolic dysregulation as seen in adults. Although the results of this exploratory, cross-sectional study are observational, it may be that the effects of concentrated disadvantage during early stages of development are not evidenced until children have transitioned to the pubertal or postpubertal period of development. This finding is consistent with a latent trajectory with regard to the life course perspective and consistent with the physiologic changes related to puberty (i.e., maturation of the HPA axis) (2,32).

The latent trajectory is one of two trajectories (latent and cumulative) which may explain, in part, the relationship between an environmental exposure to the expression of a phenotype (2,32). A latent effect indicates that the effect of an environmental exposure at one stage is not immediately evidenced but emerges at a later stage. For example, Gunnar and Quevedo (12) suggest childhood is a protected life stage with regard to stressful effects of environment possibly due to an immature HPA axis whereby the altered gene expression will only emerge once the HPA axis matures (e.g., adrenarche) (12). In contrast, a cumulative effect indicates that the effect of the environmental exposure gradually impacts emergence of the phenotype. For example, Cole (13) states that some gene expression is recursively stimulated by its own products and therefore may self-propagate once initiated by external environmental stimuli. Few studies have attempted to explicitly test these effects among the appropriate sample (e.g., prepubertal youth) and using the appropriate measures.

The observation that percent black is one of the components of CDI prompted a deconstructed analysis of the various components of the index. Interestingly, percent female-headed households tended to be the strongest factor inversely associated with the various inflammatory and metabolic markers. This sensitivity analysis provides some assurance that the inclusion of percent black in the CDI did not bias the results.

There are a number of limitations in this study, one of which is the small sample of participants due to the challenges of implementing the study in young children (ages 7–9 years). Our study used accurate, state-of-the-art methods (VAT and SAT by MRI; BF by dual-energy X-ray absorptiometry, etc.) to assess obesity and metabolic biomarkers which, due to their intensive nature, resulted in missing data. As expected, missing data occurred more frequently in intensive tests that were more difficult for children in this age group to successfully complete, compared to simpler measurements. Yet the inclusion of such advanced measures and methods is a strength, as the use of these measures in a cohort of otherwise healthy, exclusively prepubertal (<2 Tanner) black and white children with and without obesity, age 7–9 years, has only previously been reported in a few studies (19,20,31). Despite the small sample, statistically significant correlations that warrant further investigation were observed. Another limitation is the use of 2000, rather than 2010 U.S. Census data, to calculate the CDI. Prepubertal study participants, 7–9 years of age, were enrolled in the study between 2005 and 2010. At this time, all would have been exposed to environments characterized by 2000 census data during early prepubertal development. Conversely, by the year 2010 some of the participants who enrolled in the study during the first few years would have already transitioned into the pubertal and postpubertal stage of development. Our participants were classified as exclusively prepubertal using standard physician examination (Tanner staging); thus, the time of exposure should align with this period of development to accurately examine potential health outcomes. In addition, the level of exposure, that is, the number of years the participant resided in the neighborhood (i.e., census tract) from which census data were extracted to calculate concentrated disadvantage is unknown. Lastly, because this was a cross-sectional, observational study, it is not possible to demonstrate a causal relationship between CDI and inflammatory and metabolic biomarkers. Therefore, prospective studies are imperative to unraveling the complex sequence by which stressors during early childhood impact inflammatory and metabolic health outcomes later in life.

Conclusion

Chronic stress during early childhood is not associated with an impaired metabolic and inflammatory profile. Thus, children may be protected from negative health outcomes promoted by neighborhood environmental stressors prior to puberty. There are racial differences in the extent, but not the direction, of these relationships. Childhood and early adolescence marks a critical period in the life course characterized by plasticity in genomic expression that can be affected by environmental conditions. This may ultimately result in an adult phenotype associated with a variety of chronic diseases. Longitudinal studies in developing youth are needed to determine the effect of timing of exposure to stress throughout the life course on the emergence of the inflammatory and metabolic changes associated with cardio-metabolic disorders.

Acknowledgments

Funding agencies: This work was supported by the Mid-South Transdisciplinary Collaborative Center for Health Disparities Research (Mid South TCC) funded by the National Institute of Minority Health and Health Disparities (NIMHD) (U54MD008176), by the Schools of Public Health and Medicine, Department of Pediatrics, Louisiana State University Health Sciences Center in New Orleans, the Louisiana State University Health Sciences Center

School of Public Health Jim Finks Endowed Chair in Health Promotion Research Fund, The Louisiana Cancer Research Center, The Nutrition Obesity Research Center at Pennington Biomedical Research Center, and NIDDK (CNRU) 1P30 DK072476 and R01 HD49046.

References

1. Shonkoff JP, Boyce WT, McEwen BS. Neuroscience, molecular biology, and the childhoodroots of health disparities: building a new framework for health promotion and disease prevention. JAMA. 2009; 301:2252–2259. [PubMed: 19491187]
2. Hertzman C, Boyce T. How experience gets under the skin to create gradients in developmental health. Annu Rev Public Health. 2010; 31:329–347. [PubMed: 20070189]
3. Hunter RG, McEwen BS. Stress and anxiety across the lifespan: structural plasticity and epigenetic regulation. Epigenomics. 2013; 5:177–194. [PubMed: 23566095]
4. Bateson P, Barker D, Clutton-Brock T, et al. Developmental plasticity and human health. Nature. 2004; 430:419–421. [PubMed: 15269759]
5. Gluckman PD, Hanson MA, Cooper C, Thornberg KL. Effect of in utero and early-life conditions on adult health and disease. N Engl J Med. 2008; 359:61–73. [PubMed: 18596274]
6. Lawlor DA. The developmental origins of health and disease: where do we go from here? Epidemiology. 2008; 19:206–208. [PubMed: 18277159]
7. Juster RP, Bizik G, Picard M, et al. A transdisciplinary perspective of chronic stress in relation to psychopathology throughout life span development. Dev Psychopathol. 2011; 23:725–776. [PubMed: 21756430]
8. Miller GE, Chen E, Parker KJ. Psychological stress in childhood and susceptibility to the chronic diseases of aging: moving toward a model of behavioral and biological mechanisms. Psychol Bull. 2011; 137:959–997. [PubMed: 21787044]
9. Godfrey KM, Lillycrop KA, Burge GC, Gluckman PD, Hanson MA. Epigenetic mechanisms and the mismatch concept of the developmental origins of health and disease. Pediatr Res. 2007; 61:5R–10R.
10. Kuzawa CW, Sweet E. Epigenetics and the embodiment of race: developmental origins of US racial disparities in cardiovascular health. Am J Hum Biol. 2009; 21:2–15. [PubMed: 18925573]
11. Essex ML, Boyce WT, Hertzman C, et al. Epigenetic vestiges of early developmental adversity: childhood stress exposure and DNA methylation in adolescence. Child Dev. 2013; 84:58–75. [PubMed: 21883162]
12. Gunnar M, Quevedo K. The neurobiology of stress and development. Annu Rev Psychol. 2007; 58:145–173. [PubMed: 16903808]
13. Cole W. Social regulation of human gene expression: mechanisms and implications for public health. Am J Public Health. 2013; 103:S84–S92. [PubMed: 23927506]
14. Kielcolt-Glasner JK, Gouin JP, Weng NP, Malarkey WB, Beversdorf DQ, Glasner R. Childhood adversity heightens the impact of later-life caregiving stress on telomere length and inflammation. Pyschosom Med. 2011; 73:16–22.
15. Vamosi M, Heitmann BL, Kyvik KO. The relation between an adverse psychological and social environment in childhood and the development of adult obesity: a systematic literature review. Obes Rev. 2010; 11:177–184. [PubMed: 19656308]
16. Gillman MW, Rifas-Shiman SL, Kleinman K, Oken E, Rich-Edwards JW, Taveras EM. Developmental origins of childhood overweight: potential public health impact. Obesity. 2008; 16:1651–1656. [PubMed: 18451768]
17. Donoho CJ, Weigensberg MJ, Emken BA, Hsu JW, Spruijt-Metz D. Stress and abdominal fat: preliminary evidence of moderation by the cortisol awakening response in Hispanic peripubertal girls. Obesity. 2011; 19:946–952. [PubMed: 21127479]
18. Hankin BL, Badanes LS, Abela JRZ, Watamura SE. Hypothalamic pituitary adrenal axis dysregulation in dysphoric children and adolescents: cortisol reactivity to psychosocial stress from preschool through middle adolescence. Biol Psychiatry. 2010; 68:484–490. [PubMed: 20497900]

19. Bennett B, Larson-Meyer DE, Ravussin E, et al. Impaired insulin sensitivity and elevated ectopic fat in healthy obese vs. nonobese prepubertal children. Obesity. 2012; 20:371–375. [PubMed: 21869763]
20. Larson-Meyer DE, Newcomer BR, Ravussin E, et al. Intrahepatic and intramyocellular lipids are determinants of insulin resistance in prepubertal children. Diabetologia. 2011; 54:869–875. [PubMed: 21181394]
21. Tanner, JM. Growth at Adolescence; with a general consideration of the effect of hereditary and environmental factors upon growth and maturation from birth to maturity. 2nd edn.. Blackwell Scientific Publications; Oxford, UK: 1962.
22. Neovius M, Linne Y, Barkeling B, Rossner S. Discrepancies between classification systems of childhood obesity. Obes Rev. 2004; 5:105–114. [PubMed: 15086864]
23. Cutfield WS, Jefferies CA, Jackson WE, Robinson EM, Hofman PL. Evaluation of HOMA and QUICKI as measures of insulin sensitivity in prepubertal children. Pediatr Diabetes. 2003; 4:119–125. [PubMed: 14655269]
24. Lee S, Janssen I, Ross R. Interindividual variation in abdominal subcutaneous and visceral adipose tissue: influence of measurement site. J Appl Physiol. 2004; 97:948–954. [PubMed: 15121737]
25. Matthews DR, Hosker JP, Rudenski AS, Naylor BA, Treacher DF, Turner RC. Homeostasis model assessment: insulin resistance and beta-cell function from fasting plasma glucose and insulin concentrations in man. Diabetologia. 1985; 28:412–419. [PubMed: 3899825]
26. Tompkins CL, Cefalu W, Ravussin E, et al. Feasibility of intravenous glucose tolerance testing prior to puberty. Int J Pediatr Obes. 2010; 5:51–55. [PubMed: 19579147]
27. Kim SH, Sierra RA, McGee DJ, Zabaleta J. Transcriptional profiling of gastric epithelial cells infected with wild type or arginase-deficient Helicobacter pylori. BMC Microbiol. 2012; 12:175. [PubMed: 22889111]
28. Sampson RJ, Raudenbush SW, Earls F. Neighborhoods and violent crime: a multilevel study of collective efficacy. Science. 1997; 277:918–924. [PubMed: 9252316]
29. Hamilton CM, Strader LC, Pratt JG, et al. The PhenX Toolkit: Get the most from your measures. Am J Epidemiol. 2011; 174:253–260. [PubMed: 21749974]
30. Sampson RJ, Morenoff JD, Gannon-Rowley T. Assessing “Neighborhood Effects”: Social processes and new directions in research. Annu Rev Sociol. 2002; 28:443–478.
31. Zabaleta J, Velasco-Gonzalez C, Estrada J, et al. Inverse correlation of serum inflammatory markers with metabolic parameters in healthy, Black and White prepubertal youth. Int J Obes. 2014; 38:563–568.
32. Lindstrom M, Fridh M, Rosvall M. Economic stress in childhood and adulthood, and poor psychological health: three life course hypotheses. Psychiatry Res. 2014; 215:386–393. [PubMed: 24332463]

TABLE 1

Descriptive statistics for age and inflammatory and metabolic markers overall and by race

	Total				White				Black				
	N	Mean	Median	Min, Max	*N*	Mean	Median	Min, Max	*N*	Mean	Median	Min, Max	*P*-value
Age (yrs)	96	8.06	8.00	7.00, 9.00	70	8.09	8.00	7.00, 9.00	26	8.00	8.00	7.00, 9.00	0.63
z_BMI	96	1.06	1.07	−1.56, 2.88	70	0.98	0.94	−1.04, 2.88	26	1.28	1.45	−1.56, 2.86	0.20
Body fat	95	10.41	8.06	3.05, 53.38	69	9.81	7.99	3.05, 53.38	26	11.99	8.47	3.20, 29.20	0.20
VAT	74	13.07	11.51	3.02, 35.97	58	13.15	11.62	3.02, 35.97	16	12.78	11.18	4.122, 22.88	0.85
SAT	74	138.5	101.1	19.34, 797.5	58	129.3	96.11	19.34, 797.5	16	171.9	112.9	22.82, 461.4	0.24
HOMA-IR	68	0.84	0.58	0.07, 6.03	48	0.62	0.51	0.07, 2.37	20	1.35	0.89	0.08, 6.03	0.001
IMCL	90	0.01	0.01	0.001, 0.02	67	0.001	0.001	0.001, 0.02	23	0.01	0.01	0.001, 0.02	0.15
IHL	84	0.01	0.01	0.001, 0.05	62	0.01	0.01	0.001, 0.03	22	0.01	0.01	0.001, 0.05	0.75
IL-6	37	188.7	2.06	0.69, 4673	27	257.7	2.3	0.69, 4674	10	2.27	1.68	1.12, 6.09	0.39
IL-8	37	847.8	3.83	1.31, 15,007	27	1158.7	3.79	1.76, 15007	10	8.33	3.85	3.78, 14.78	0.30
TNF-α	37	4.92	1.23	0.61, 69.58	27	5.91	1.12	0.61, 69.58	10	2.25	1.11	0.87, 4.58	0.42
Male (%)	51	53.13	–	–	37	52.86	–	–	14	53.85	–	–	0.93

TABLE 2

Spearman correlation (ρ) between CDI and inflammatory and metabolic markers overall and by race

	Total[a]			White[b]			Black[b]		
	N	ρ	*P*-value	*N*	ρ	*P*-value	*N*	ρ	*P*-value
z_BMI	96	−0.234	0.023[c]	70	−0.269	0.025[c]	26	−0.095	0.652
Body fat	95	−0.228	0.028[c]	69	−0.293	0.015[c]	26	−0.041	0.848
VAT	74	−0.241	0.042[c]	58	−0.280	0.035[c]	16	−0.103	0.715
SAT	74	−0.227	0.055	58	−0.294	0.026	16	0.014	0.962
HOMA-IR	68	0.050	0.691	48	0.022	0.885	20	0.233	0.338
IMCL	90	−0.139	0.196	67	−0.161	0.195	23	−0.071	0.752
IHL	84	0.058	0.606	62	−0.012	0.924	22	0.252	0.271
IL-6	37	−0.117	0.503	27	−0.010	0.962	10	−0.357	0.345
IL-8	37	−0.221	0.201	27	−0.120	0.560	10	−0.551	0.124
TNF-α	37	0.054	0.757	27	−0.036	0.860	10	0.175	0.652

[a] CDI is partialed for race and sex.

[b] CDI is partialed for sex.

[c] *P*-value <0.05.

TABLE 3

Spearman correlation between concentrated disadvantage individual variables and inflammatory and metabolic markers overall and by race

	n	% Unemployment, *ρ*	% Black, *ρ*	% Female head of house, *ρ*	% Poverty, *ρ*	% Receive public assistance *ρ*	% Under 18 years, *ρ*
z_BMI	**96**	−0.195	−0.084	−0.263[a]	−0.099	−0.084	0.068
Body fat	**95**	−0.207	−0.025[a]	−0.275[a]	−0.103	−0.049	0.128
VAT	**74**	−0.140	−0.023	−0.345[a]	−0.030	0.005	0.245[a]
SAT	**74**	−0.129	−0.001	−0.330[a]	−0.067	−0.023	0.218
HOMA-IR	**68**	0.104	0.162	−0.082	0.214	0.182	0.025
IMCL	**90**	−0.147	−0.013	−0.177	−0.060	−0.009	0.112
IHL	**84**	0.013	0.048	0.039	0.047	0.030	−0.030
IL-6	**37**	−0.096	0.010	−0.124	−0.132	−0.258	0.167
IL-8	**37**	−0.180	−0.165	−0.211	−0.156	−0.298	−0.039
TNF-α	**37**	0.098	0.0230	0.038	0.030	0.084	0.089

[a] *P*-value <0.05.