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Examination of the Role of Obesity in the Association Between Childhood Trauma and Inflammation During Pregnancy

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Objective: Childhood trauma is associated with negative perinatal health outcomes including mood disorders and shorter gestation. However, effects of early life exposures on maternal biology are poorly delineated. This study examined associations between childhood trauma and inflammation, as well as the mediating role of obesity in this relationship. ***Method:*** This study examined a racially diverse sample of 77 pregnant women assessed in early, mid, and late pregnancy. Assessments included the Childhood Trauma Questionnaire, Center for Epidemiologic Studies-Depression Scale, serum CRP, IL-6, and TNF-α, and prepregnancy BMI. ***Results:*** Per linear mixed models, while no direct relationships were observed between childhood trauma with IL-6 or TNF-α, physical (95% CI: 0.007, 0.080) and emotional (95% CI: 0.005, 0.046) abuse as well as emotional neglect (95% CI: 0.010, 0.051) predicted elevated CRP. Effects remained after adjustment for race, income, education, smoking status, medical conditions, and depressive symptoms. PROCESS analyses showed BMI mediated the relationship between physical abuse and both serum CRP (95% CI: 0.014, 0.062) and IL-6 (95% CI: 0.009, 0.034). ***Conclusions:*** Exposure to childhood trauma, particularly emotional abuse, physical abuse, and emotional neglect, is associated with inflammation in pregnant women. Obesity served as 1 pathway by which physical abuse contributed to elevations in serum CRP and IL-6. Interventions targeting maternal obesity prior to pregnancy may help mitigate the effects of childhood trauma on perinatal health. These findings have relevance for understanding biological and behavioral pathways by which early life exposures contribute to maternal health.

Keywords: BMI, C-reactive protein (CRP), childhood trauma, interleukin (IL) 6, pregnancy, tumor necrosis factor (TNF) α

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In the United States, 1 in 4 children under age 18 have experienced some type of abuse or neglect (Finkelhor, Turner, Shattuck, & Hamby, 2013). A substantial body of literature shows a strong and consistent relationship between early life trauma and adverse health outcomes in adulthood, such as depression, migraines, arthritis, strokes, and asthma, with greater effects found in women (Andrea Danese et al., 2009; Leeb, Lewis, & Zolotor, 2011; Wegman & Stetler, 2009). In addition, childhood trauma may negatively contribute to perinatal health, including antepartum and postpartum depression, anxiety, and birth outcomes (Choi & Sikkema, 2016; Smith, Gotman, & Yonkers, 2016; Wosu, Gelaye, & Williams, 2015). For example, Smith and colleagues found that, in a sample of 2,303 pregnant women, each adverse childhood experience was associated with a 16.33*g* reduction in birth weight as well as a 0.063 week decrease in gestational age at delivery (2016). Despite these associations, the relationship between early life exposures and maternal biology during pregnancy has received limited attention.

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Consistent with psychobiological models (e.g., Miller, Chen, & Parker, 2011), a key process affected by childhood trauma resulting in increased adult health risk is inflammation. A meta-analysis of 25 studies with ≥881 nonpregnant adults per inflammatory parameter showed that childhood trauma was associated with elevated C-reactive protein (CRP), interleukin (IL)-6, and tumor necrosis factor (TNF)-α (Baumeister, Akhtar, Ciufolini, Pariante, & Mondelli, 2016). These effects have been found in both cross-sectional and longitudinal data (Danese, Pariante, Caspi, Taylor, & Poulton, 2007; Matthews, Chang, Thurston, & Bromberger, 2014); for example, a study of 972 adults showed that those who experienced one or more indicators of early life trauma exhibited 1.18 to 1.80 greater odds of exhibiting clinically significant CRP levels (>3 mg/L) 20 years later, compared with those with no trauma history (Danese, et al., 2007).

Inflammation has unique relevance for perinatal health; elevations in inflammatory markers during pregnancy have been linked to shorter gestation/preterm birth (Blair, Porter, Leblebicioglu, & Christian, 2015; Coussons-Read et al., 2012) as well as depressive symptoms (Christian, Franco, Glaser, & Iams, 2009). There are significant increases in hormones associated with the hypothalamic-pituitary-adrenal (HPA) axis across the course of pregnancy (Glynn, Schetter, Chicz-DeMet, Hobel, & Sandman, 2007) and glucocorticoids play a key role in regulating immune functioning (Baumeister et al., 2016; Elenkov & Chrousos, 2002). This is consistent with data showing considerable changes in serum inflammatory markers during pregnancy (Christian & Porter, 2014; Coussons-Read, Okun, & Nettles, 2007; Glynn et al., 2007). Given such pronounced maternal physiological adaptation across pregnancy, it is possible that the link between childhood trauma and inflammation may not be as evident in pregnancy. Data on trauma and inflammation specifically in pregnant women are limited. In a sample of 145 women, lifetime trauma history, although not childhood specific, was associated with elevated serum tumor necrosis factor TNF-alpha but not IL-6 in mid- and late pregnancy (Blackmore et al., 2011). In addition, among 133 adolescents, greater exposure to childhood trauma was associated with elevated IL-6 in midpregnancy, but only among those with high depressive symptoms and no associations with C-reactive protein (CRP) were observed (Walsh et al., 2016). Additional data from pregnant women across the course of gestation would be informative.

As posited in a model of psychoneuroimmunology during pregnancy, health behaviors likely play a mediating role in the relationship between childhood trauma and inflammation (Christian, 2012). Of clinical relevance, a meta-analysis of 41 studies showed that individuals who experienced childhood trauma had 1.36 greater odds of becoming obese during their lifetime compared with those who did not (A Danese & Tan, 2014). Given that adipocytes secrete proinflammatory markers, including IL-6 and TNF-α, and IL-6 modulates hepatic CRP production, obesity is one potential pathway by which early life exposures may contribute to elevated inflammatory markers (Bastard et al., 2006; Denison, Roberts, Barr, & Norman, 2010; Maachi et al., 2004). For example, a study of 326 nonpregnant women found that childhood trauma was associated with serum CRP levels via increased body mass index (BMI) (Matthews et al., 2014). Despite substantial changes in inflammation across pregnancy, obesity prior to pregnancy is associated with elevations in serum CRP, IL-6, and TNF-α (Christian & Porter, 2014). Thus, examination of the potential mediating role of prepregnancy BMI in the relationship between childhood trauma and inflammation in pregnant women is warranted.

Addressing gaps in the literature, the current study examined associations of self-reported childhood trauma (i.e., abuse/neglect) with serum CRP, IL-6, and TNF-α in a racially diverse sample of 77 pregnant women assessed in early, mid, and late pregnancy. It was hypothesized that (a) greater childhood trauma would be associated with elevated serum CRP, IL-6, and TNF-α independent of race, income, education, smoking status, and depressive symptoms and (b) prepregnancy BMI would play a mediating role in these associations.

Method

Study Design and Participants

Eighty-four women were recruited from the Ohio State University Wexner Medical Center (OSUWMC) Prenatal Clinic and the community of Columbus, Ohio. Data collection occurred from 2011 to 2014. The broader study collected blood samples and assessed psychosocial stress across pregnancy and postpartum. Blood samples and psychosocial data were collected in early, mid, and late pregnancy.

Women were ineligible if they had any known fetal anomaly, illicit drug use, consumption of more than two alcohol drinks per week during pregnancy (per self-report or medical record), or major immunological or endocrine conditions (e.g., rheumatoid arthritis, hypothyroidism). Women who described experiencing acute illness within 10 days of a study visit were rescheduled. The current analyses included women who participated in at least two study visits, including the third visit at which childhood trauma was assessed; seven women were excluded because they did not meet these criteria, resulting in a final analytic sample of 77. Written informed consent was obtained at the first study visit, and participants received modest financial compensation at the completion of each visit. The study was approved by the OSU Biomedical Institutional Review Board.

Measures

Demographics. Race/ethnicity, age, marital status, annual household income, education level, and number of prior births (parity) were collected by self-report at the first study visit. Adverse outcomes (i.e., gestational hypertension, preeclampsia, and gestational diabetes) were obtained per medical record review. Prepregnancy BMI (kg/m^2) was calculated utilizing self-reported prepregnancy weight and measured height at the first visit. Although self-reported BMI tends to be lower than measured BMI, these relationships are strongly correlated in reproductive-aged women (r = .90–0.99) (Roth, Allshouse, Lesh, Polotsky, & Santoro, 2013; Shin, Chung, Weatherspoon, & Song, 2014; Spencer, Appleby, Davey, & Key, 2002). In addition, in a sample of 10,639 adults, self-reported BMI and measured BMI were similarly associated with various biomarkers, including CRP (McAdams, Van Dam, & Hu, 2007).

Health behaviors. Smoking, exercise, and prenatal vitamin use were assessed via self-report at the first study visit. Smoking was defined as current or not current at the time of the visit.

Regarding exercise, participants responded to an item assessing the current frequency with which they engaged in a vigorous activity long enough to build up a sweat at the time of the visit. Prenatal vitamin use was operationalized as never, 1–3 days per week, 4–6 days per week, or 7 days per week since pregnancy was known.

Childhood trauma. The 28-item Childhood Trauma Questionnaire (CTQ) includes 5 subscales: emotional abuse, physical abuse, sexual abuse, emotional neglect, and physical neglect (D. P Bernstein et al., 2003). Respondents rated each item on a 5-point scale, from *Never true* to *Very often true*. This measure has good criterion, convergent, and discriminant validity in adults and adolescents (D. P Bernstein et al., 2003). In addition, the CTQ has shown predictive validity for perinatal health outcomes (Möhler et al., 2008; Shea et al., 2007). In the current study, the CTQ was administered at the third visit to reduce respondent burden in earlier visits and increase opportunities to build rapport with participants.

Depressive symptoms. The Center for Epidemiologic Studies Depression Scale (CES-D) was administered at each visit to assess depressive symptoms. This scale comprises 20 items assessing cognitive, emotional, interpersonal, and somatic depressive symptoms (Radloff, 1977). The CES-D has been shown to exhibit scores which are reliable and valid in predicting physiological processes as well as health outcomes in pregnancy (Christian et al., 2009; Christian, Franco, Iams, Sheridan, & Glaser, 2010; Li, Liu, & Odouli, 2009; Phillips, Wise, Rich-Edwards, Stampfer, & Rosenberg, 2010).

Blood parameters. Blood was collected into vacutainer tubes primarily between the hours of 9:30am and 12:30 p.m. (99.1% of draws) while participants were in a seated position. Samples were immediately centrifuged, aliquoted, and placed in −80°C freezer storage until analysis. CRP was measured using chemilluminescence methodology with an Immulite 1000 (Siemens Healthcare Diagnostics, Inc., Deerfield, IL). The kit uses a solid phase chemilluminescence immunometric assay. The solid phase (bead) is coated with antiligand; the liquid phase consists of ligand labeled anti-CRP murine monoclonal antibody and alkaline phosphatase (bovine calf intestine) conjugated to rabbit polyclona l anti-CRP antibody in buffer. This is manufactured specifically for this equipment. Analytical sensitivity and function sensitivity for this assay was 0.01 mg/L and 0.3 mg/L, respectively. Intraassay coefficient of variation was 3.1% and interassay coefficient variation was 7.3%.

Serum levels of IL-6 and TNF-α were assayed in single spot ultrasensitive or multiplex V-Plex kits from Meso Scale Discovery (MSD, Meso Scale Discovery, 1601 Research Blvd, Rockville, MD). Plates were read by an MSD SECTOR Imager 2400 measuring electrochemiluminescence. Sample concentrations were extrapolated from a standard curve calculated using a four parameter logistic fit with MSD Workbench 3.0 software. The limit of detection was 0.31 pg/mL and 0.17 pg/mL for IL-6 and TNF-α, respectively. Inter- and intraassays coefficients of variation were 8.69% and 5.89% for IL-6 and 6.02% and 2.36% for TNF-α.

Statistical Analyses

All analyses were conducted in SPSS 22.0 and SAS 9.4. Missing data were addressed utilizing the restricted maximum likelihood estimation method. Serum CRP, IL-6, and TNF-α were log-transformed (base 10) to fit the normality assumption. Descriptive statistics were calculated for all participants.

Linear mixed models were conducted to examine the effect of childhood trauma on CRP, IL-6, and TNF-α levels across gestational weeks. Plots and model fit indices (Müller, Scealy, & Welsh, 2013) were reviewed to determine the functional form for time (i.e., gestational weeks) parameter(s) and error structures for repeated measures which provided the best model fit. CRP levels were modeled using quadratic and linear time parameters, an autoregressive heterogeneous error structure, and a subject-level random intercept; IL-6 levels were modeled using a linear time parameter, an autoregressive heterogeneous error structure, and a subject-level random intercept; TNF-α levels were modeled using a linear time parameter, an autoregressive error structure, and a subject-level random intercept. An interaction term between the highest order time parameter and childhood trauma was investigated and removed if not statistically significant.

After establishing the time function and error structure, each model was adjusted for race, income, education, smoking status, medical conditions (i.e., gestational hypertension, preeclampsia, and gestational diabetes), and depressive symptoms; these covariates were selected a priori per evidence in the literature (Christian et al., 2009; Christian, Glaser, Porter, & Iams, 2013; Ford et al., 2011; Friedman & Herd, 2010; Gillespie, Porter, & Christian, 2016; Hatch & Dohrenwend, 2007; Scher, Forde, McQuaid, & Stein, 2004). All tests were evaluated at $p < .05$ level of significance using 95% confidence intervals (CI).

To demonstrate whether effects of childhood trauma on inflammation emerged after adjustment for BMI (a preliminary test of BMI as a mediator) model statistics were examined with and without BMI. To further examine the potential mediating role of BMI in the relationship between childhood trauma and inflammatory markers after adjustment for race, income, education, smoking status, medical conditions (i.e., gestational hypertension, preeclampsia, and gestational diabetes), and baseline depressive symptoms, the widely used approach posited by Preacher and Hayes was employed (Preacher & Hayes, 2008). PROCESS macros were used to estimate indirect effects and bias-corrected 95% bootstrap confidence intervals (CI) based on 10,000 bootstrap samples were examined to determine statistical significance (Hayes, 2013). Bootstrap samples are replaced when necessary in PROCESS; this occurred with less than 1% of samples in each model. As there were no significant interactions between time and childhood trauma, the mean value for each inflammatory marker across pregnancy served as the outcome variable for each mediation analysis.

Results

Sample Characteristics

Study visits occurred in early (mean gestational age = 12.45, *SD* = 1.57 weeks), mid (mean gestational age = 20.63, *SD* = 1.30 weeks), and late pregnancy (mean gestational age = 29.21, *SD* = 1.41 weeks). Demographic characteristics, health behaviors, and trauma variables for the total sample are detailed in Table 1. The average maternal age was 25.58 years (*SD* = 4.14, range: 18–33), 51% (*n* = 39) were White (including one woman who endorsed

Table 1
Demographics, Health Characteristics, and Trauma Variables

Variable	$n = 77$
Age [Mean (*SD*)]	25.58 (4.1)
Race [*n* (%)]	
White	39 (50.6)
Black	38 (49.4)
Marital status [*n* (%)]	
Married	32 (41.6)
In a relationship	35 (45.5)
Single	10 (13.0)
Education [*n* (%)]	
Less than high school or high school graduate	19 (24.7)
Some college	31 (40.3)
College degree	27 (35.1)
Income [*n* (%)]	
<$15,000	23 (29.9)
$15,000–29,999	22 (28.6)
>$30,000	32 (41.6)
Parity (# of prev. births) [*n* (%)]	
0	24 (31.2)
1	28 (36.4)
2 or more	25 (32.5)
Smoking status [*n* (%)]	
Current	8 (10.4)
Not current or never	69 (89.6)
Exercise [*n* (%)]	
Once or less than once per month	30 (39.0)
2–3 times per month	21 (27.3)
Once or more than once per week	26 (33.8)
Prenatal vitamin use [*n* (%)]	
Never or some days (0–3/week)	17 (22.1)
Most or every day (4–7/week)	60 (77.9)
Medical conditions[a] [*n* (%)]	5 (6.5)
CES-D [Mean (*SD*)]	
Early pregnancy	15.7 (10.6)
Mid pregnancy	11.1 (7.3)
Late pregnancy	10.16 (6.6)
BMI [Mean (*SD*)]	27.4 (6.1)
BMI Category [*n* (%)]	
Normal	33 (42.9)
Overweight	24 (31.2)
Obese	20 (26.0)
Abuse and neglect [Mean (*SD*)]	
Emotional abuse	7.6 (4.1)
Physical abuse	6.2 (5.0)
Sexual abuse	7.0 (5.0)
Emotional neglect	8.8 (8.0)
Physical neglect	7.0 (6.0)

Note. CES-D = Center for Epidemiologic Studies – Depression Scale; BMI = Pre pregnancy body mass index.
[a] Medical conditions include hypertension, preeclampsia, and gestational diabetes.

Hispanic ethnicity), and 58% ($n = 45$) reported an income of less than $30,000.

CRP, IL-6, and TNF-α Across Pregnancy

Means (*SD*), medians (IQR), and model adjusted means for each inflammatory marker in early, mid, and late pregnancy are described in Table 2. In the overall sample, a significant quadratic effect was observed with CRP, $F(1, 122) = 4.68$, $p = .03$ over time. With regard to TNF-α and IL-6, in this study sample, we have previously reported a significant increase in TNF-α between early and midpregnancy, with no change from mid- to late pregnancy, as well as no observable change in IL-6 over time (Mitchell, Palettas, & Christian, 2017).

Childhood Trauma Exposure and CRP

Linear mixed models were conducted to examine whether exposure to childhood abuse or neglect was associated with CRP levels across pregnancy. As depicted in Table 3, in Type I models, main effects were found for emotional abuse (95% CI: 0.005, 0.046), physical abuse (95% CI: 0.007, 0.080), and emotional neglect (95% CI: 0.010, 0.051), with greater trauma exposure associated with higher levels of CRP. These effects remained after adjusting for income, race, education, smoking status, medical conditions, and depressive symptoms in Type II models. However, as hypothesized, with the addition of BMI in Type 3 models, the effects of emotional abuse (95% CI: −0.005, 0.033) and physical abuse (95% CI: −0.027, 0.039) were no longer significant, supporting a mediating role for BMI in the association between childhood trauma and elevated CRP (see Table 4). The main effect of emotional neglect was reduced with the inclusion of BMI although it remained significant (95% CI: 0.001, 0.036).

Childhood Trauma Exposure and IL-6

Next, linear mixed models were conducted to examine whether exposure to abuse or neglect affected IL-6 levels across pregnancy. As shown in Table 3, in Type I models, no significant effects were observed on IL-6 in relation to CTQ subscales: emotional abuse (95% CI: −0.006, 0.019), physical abuse (95% CI: −0.007, 0.046), sexual abuse (95% CI: −0.009, 0.013), emotional neglect (95% CI: −0.004, 0.021), and physical neglect (95% CI: −0.024, 0.015).

Childhood Trauma Exposure and TNF-α

Finally, linear mixed models were conducted to examine whether exposure to abuse or neglect affected TNF-α across pregnancy. As described in Table 3, in Type I models, no significant effects were observed on TNF-α in relation to CTQ subscales: emotional abuse (95% CI: −0.008, 0.002), physical abuse (95% CI: −0.009, 0.008), sexual abuse (95% CI: −0.007, 0.001), emotional neglect (95% CI: −0.006, 0.004), and physical neglect (95% CI: −0.010, 0.004).

BMI as a Mediator

As described, some of the above models supported a mediating role for obesity in linking childhood trauma and inflammation; thus, more robust analyses of mediation were conducted using PROCESS (Hayes, 2013). PROCESS models were examined for each model, given that an indirect effect can be present in the absence of a significant total effect (Hayes, 2009). In these analyses, race, income, education, smoking status, medical conditions, and depressive symptoms in early pregnancy were included as covariates. Per PROCESS, as shown in Table 5, BMI served as significant mediator in the relationship between physical abuse and both CRP (95% CI: 0.014, 0.062) and IL-6 (95% CI: 0.009, 0.034). Significant indirect effect findings remained when the respective inflammatory marker at each timepoint was used

Table 2
Inflammatory Markers Across Pregnancy

Marker	Raw means (*SD*)	Raw medians (IQR)	Model adjusted means (95% CI)[a]
C-reactive protein			
Early pregnancy	10.1 (13.5)	6.4 (3.0–11.2)	6.1 (4.9, 7.6)
Mid pregnancy	12.0 (7.6)	7.6 (3.7–15.8)	6.8 (5.4, 8.6)
Late pregnancy	8.5 (5.3)	8.8 (2.9–9.6)	5.8 (4.7, 7.0)
Interleukin 6			
Early pregnancy	.89 (.59)	.71 (.49–1.13)	.74 (.65, .85)
Mid pregnancy	1.1 (1.3)	.75 (.47–1.20)	.77 (.68, .87)
Late pregnancy	.92 (.55)	.77 (.53–1.19)	.80 (.71, .90)
Tumor necrosis factor α			
Early pregnancy	2.1 (.41)	2.1 (1.9–2.4)	2.11 (2.02, 2.21)
Mid pregnancy	2.4 (.62)	2.3 (2.0–2.6)	2.16 (2.08, 2.25)
Late pregnancy	2.2 (.37)	2.3 (2.0–2.5)	2.22 (2.13, 2.32)

Note. Values were log-transformed for analyses.
[a] Least square means at midpoint of each assessment (12, 20, and 29 weeks), back-transformed to the original scale with 95% confidence intervals.

rather than an average value across pregnancy, with the exception of one model which had a lower confidence interval value of 0. BMI did not serve as a mediator in other models (see Table 5).

Discussion

In the current study of pregnant women, exposure to physical abuse as well as emotional abuse and neglect predicted elevated CRP. These effects remained after adjustment for race, income, education, smoking status, medical conditions, and depressive symptoms. These findings extend upon studies linking childhood trauma with elevated CRP and IL-6 in nonpregnant adults (Baumeister et al., 2016; Danese et al., 2008; Danese, et al., 2007; Kiecolt-Glaser et al., 2011; Matthews et al., 2014; Slopen et al., 2010). In contrast, the association between childhood trauma and TNF-α was not replicated (Baumeister et al., 2016). As reviewed, such data in pregnant women are limited. Among 145 racially diverse women assessed at mid and late pregnancy, greater lifetime exposure to traumatic events, per clinical interview, was associated with elevated serum TNF-α, but not IL-6 (Blackmore et al., 2011). In addition, among 133 Latina adolescents assessed at mid and late pregnancy, an interaction between child abuse exposure and depression was observed in predicting serum IL-6 (Walsh et al., 2016). The current study demonstrates effects of childhood trauma on inflammation across gestation among Black and White women who were predominately low income.

Table 3
Type 1 and 2 Linear Mixed Models for All Inflammatory Markers

	Type 1			Type 2		
Marker	*F* (*df*)	Estimate (*SE*)	95% CI	*F* (*df*)	Estimate (*SE*)	95% CI
CRP						
Emotional abuse	6.19 (1, 75)	.03 (.01)	(.005, .046)[a]	7.10 (1, 70)	.03 (.01)	(.007, .052)[a]
Physical abuse	5.54 (1, 75)	.04 (.02)	(.007, .080)[a]	5.03 (1, 68)	.04 (.02)	(.005, .078)[a]
Sexual abuse	.74 (1. 75)	.01 (.01)	(−.011, .27)	.15 (1, 71)	.004 (.01)	(−.016, .023)
Emotional neglect	8.89 (1, 75)	.03 (.01)	(.010, .051)[a]	7.28 (1, 70)	.03 (.01)	(.008, .050)[a]
Physical neglect	2.65 (1, 75)	.03 (.02)	(−.006, .056)	1.19 (1, 68)	.02 (.02)	(−.015, .051)
IL-6						
Emotional abuse	1.10 (1, 75)	.01 (.01)	(−.006, .019)	2.83 (1, 69)	.01 (.01)	(−.002, .025)
Physical abuse	3.75 (1,74)	.02 (.01)	(−.007, .046)	3.64 (1, 66)	.02 (.01)	(−.001, .043)
Sexual abuse	.10 (1, 75)	.002 (.01)	(−.009, .013)	.03 (1, 69)	.001 (.01)	(−.011, .013)
Emotional neglect	1.81 (1, 75)	.01 (.01)	(−.004, .021)	1.92 (1, 69)	.01 (.01)	(−.004, .022)
Physical neglect	.22 (1, 74)	−.005 (.01)	(−.024, .015)	.17 (1, 66)	−.004 (.01)	(−.024, .016)
TNF-α						
Emotional abuse	1.66 (1, 75)	−.003 (.002)	(−.008, .002)	.68 (1, 68)	−.002 (.003)	(−.007, .003)
Physical abuse	.01 (1, 75)	−.0005 (.004)	(−.009, .008)	.08 (1, 67)	.001 (.004)	(−.007, .010)
Sexual abuse	2.25 (1, 75)	−.003 (.002)	(−.007, .001)	3.32 (1, 68)	−.004 (.002)	(−.010, .0004)
Emotional neglect	.19 (1, 75)	−.001 (.002)	(−.006, .004)	.001 (1, 68)	.0001 (.003)	(−.005, .005)
Physical neglect	.49 (1, 75)	−.002 (.003)	(−.010, .004)	.06 (1, 67)	−.001 (.004)	(−.008, .007)

Note. Type 1: no covariates; Type 2: income, race, education, smoking status, medical conditions, and depressive symptoms. CI = confidence interval. Time and error structures for models are detailed in text with two exceptions: type 1 physical abuse and neglect models with IL-6 used an autoregressive error structure.
[a] Significant effect.

Table 4
Final Linear Mixed Models With CRP

Variable	*F* (*df*)	Estimate (*SE*)	95% CI
Emotional abuse			
Race	.12 (1, 68)	−.03 (.07)	(−.171, .120)
Income	.39 (2, 68)	—	—
<$15,000	—	.05 (.10)	(−.158, .260)
$15,000–29,999	—	.08 (.09)	(−.101, .263)
>$30,000		Reference	
Education	.78 (2, 68)	—	—
Less than HS or HS graduate	—	.07 (.12)	(−.159, .307)
Some college	—	−.04 (.09)	(−.220, .132)
College degree		Reference	
Smoking status	.24 (1, 71)	−.06 (.12)	(−.302, .183)
Medical conditions	2.98 (1, 67)	.25 (.14)	(−.039, .534)
Depressive symptoms	.55 (1, 161)	−.002(.003)	(−.008, .004)
Pre pregnancy BMI	35.43 (1, 67)	.04 (.01)	(.024, .049)[a]
Linear time	3.65 (1, 131)	.04 (.02)	(−.002, .073)
Quadratic time	4.25 (1, 127)	−.001 (.0004)	(−.002, −.00004)[a]
Emotional abuse	2.08 (1, 70)	.01 (.01)	(−.005, .033)
Physical abuse			
Race	.46 (1, 68)	−.05 (.07)	(−.133, 1.127)
Income	.63 (2, 68)	—	—
<$15,000	—	.10 (.10)	(−.103, .299)
$15,000–29,999	—	.09 (.09)	(−.095, .274)
>$30,000		Reference	
Education	.71 (2, 68)	—	—
Less than HS or HS graduate	—	.02 (.11)	(−.205, .244)
Some college	—	−.08 (.09)	(−.250, .096)
College degree		Reference	
Smoking status	.23 (1, 71)	−.06 (.12)	(−.307, .188)
Medical conditions	2.38 (1, 67)	.22 (.14)	(−.066, .512)
Depressive symptoms	.25 (1, 157)	−.001(.003)	(−.007, .004)
Pre pregnancy BMI	35.24 (1, 68)	.04 (.01)	(.025, .051)[a]
Linear time	3.76 (1, 131)	.04 (.02)	(−.001, .074)
Quadratic time	4.30 (1, 126)	−.001 (.0004)	(−.002, −.00004)[a]
Physical abuse	.14 (1, 67)	.01 (.02)	(−.027, .039)
Sexual abuse			
Race	.46 (1, 168)	−.05 (.07)	(−.193, .095)
Income	.79 (2, 68)	—	—
<$15,000	—	.11 (.10)	(−.088, .316)
$15,000–29,999	—	.10 (.10)	(−.255, .086)
>$30,000		Reference	
Education	.68 (2, 68)	—	—
Less than HS or HS graduate	—	−.001 (.11)	(−.227, .226)
Some college	—	−.08 (.09)	(−.255, .086)
College degree		Reference	
Smoking status	.23 (1, 71)	−.06 (.12)	(−.304, .187)
Medical conditions	2.22 (1, 67)	.21 (.14)	(−.072, .502)
Depressive symptoms	.14 (1, 154)	−.001 (.003)	(−.007, .005)
Pre pregnancy BMI	43.35 (1, 67)	.04 (.01)	(.028, .052)[a]
Linear time	3.77 (1, 131)	.04 (.02)	(−.001, .074)
Quadratic time	4.29 (1, 127)	−.001 (.0004)	(−.002, −.00004)[a]
Sexual abuse	.34 (1, 71)	−.005 (.01)	(−.020, .011)
Emotional neglect			
Race	.46 (1, 68)	−.05 (.07)	(−.187, .092)
Income	.34 (2, 68)	—	—
<$15,000	—	.05 (.10)	(−.148, .251)
$15,000–29,999	—	.07 (.09)	(−.106, .252)
>$30,000		Reference	
Education	.30 (2, 68)	—	—
Less than HS or HS graduate	—	.03 (.11)	(−.191, .241)

(*table continued*)

Table 4 (*continued*)

Variable	*F* (*df*)	Estimate (*SE*)	95% CI
Some college	—	−.04 (.09)	(−.212, .128)
College degree		Reference	
Smoking status	.11 (1, 71)	−.04 (.12)	(−.279, .200)
Medical conditions	2.61 (1, 67)	.23 (.14)	(−.053, .505)
Depressive symptoms	.66 (1, 159)	−.002 (.003)	(−.008, .003)
Pre pregnancy BMI	38.64 (1, 67)	.04 (.01)	(.025, .049)[a]
Linear time	3.91 (1, 132)	.04 (.02)	(−.00004, .074)
Quadratic time	4.53 (1, 127)	−.001 (.0004)	(−.002, −.00007)[a]
Emotional neglect	4.30 (1, 69)	.02 (.01)	(.001, .036)[a]
Physical neglect			
Race	.34 (1, 68)	−.04 (.07)	(−.189, .103)
Income	.40 (2, 68)	—	—
<$15,000	—	.08 (.10)	(−.129, .290)
$15,000–29,999	—	.08 (.09)	(−.112, .263)
>$30,000		Reference	
Education	.59 (2, 68)	—	—
Less than HS or HS graduate	—	.03 (.11)	(−.195, .260)
Some college	—	−.06 (.09)	(−.241, .116)
College degree		Reference	
Smoking status	.20 (1, 71)	−.06 (.12)	(−.301, .191)
Medical conditions	2.21 (1, 67)	.21 (.14)	(−.073, .501)
Depressive symptoms	.30 (1, 158)	−.002 (.003)	(−.007, .004)
Pre pregnancy BMI	41.77 (1, 67)	.04 (.006)	(.027, .051)[a]
Linear time	3.69 (1, 132)	.04 (.02)	(−.001, .073)
Quadratic time	4.24 (1, 127)	−.001 (.0004)	(−.002, −.00004)[a]
Physical neglect	.44 (1, 68)	.01 (.01)	(−.018, .035)

Note. CI = confidence interval; HS = high school. Reference groups for dichotomous variables: white, not currently smoking, no medical conditions.
[a] Significant effect.

Based on a model of psychoneuroimmunology during pregnancy (Christian, 2015) and existing literature, the potential mediating role of prepregnancy body composition in the observed associations between trauma exposure and inflammation was of interest. Prior studies have linked childhood abuse and neglect with prepregnancy overweight and obesity (Hollingsworth, Callaway, Duhig, Matheson, & Scott, 2012; Nagl, Steinig, Klinitzke, Stepan, & Kersting, 2016; Ranchod et al., 2016). Further, data from 326 nonpregnant women demonstrated that observed associations between child abuse and neglect exposure with elevated

Table 5
Mediation Models

Mediation models	Total effect *b* (*SE*)	95% CI	Direct effect *b* (*SE*)	95% CI estimates	Indirect effect *b* (*SE*)	95% CI estimates
CRP						
Emotional abuse → BMI → CRP	.03 (.01)	(.008, .056)[a]	.02 (.01)	(−.003, .038)	.01 (.01)	(−.001, .034)
Physical abuse → BMI → CRP	.04 (.02)	(.004, .080)[a]	.01 (.02)	(−.025, .044)	.03 (.01)	(.014, .062)[a]
Sexual abuse → BMI → CRP	.01 (.01)	(−.013, .027)	−.003 (.01)	(−.020, .013)	.01 (.01)	(−.011, .029)
Emotional neglect → BMI → CRP	.03 (.01)	(.009, .053)[a]	.02 (.01)	(.004, .041)[a]	.01 (.01)	(−.007, .024)
Physical neglect → BMI → CRP	.01 (.02)	(−.021, .047)	.01 (.01)	(−.020, .036)	.01 (.02)	(−.033, .029)
IL-6						
Emotional abuse → BMI → IL-6	.01 (.01)	(−.006, .022)	−.001 (.01)	(−.013, .010)	.01 (.01)	(−.001, .020)
Physical abuse → BMI → IL-6	.02 (.01)	(−.002, .041)	.001 (.01)	(−.018, .020)	.02 (.01)	(.009, .034)[a]
Sexual abuse → BMI → IL-6	.001 (.01)	(−.010, .012)	−.01 (.005)	(−.014, .004)	.01 (.01)	(−.007, .016)
Emotional neglect → BMI → IL-6	.005 (.01)	(−.009, .018)	−.001 (.01)	(−.012, .010)	.01 (.005)	(−.004, .015)
Physical neglect → BMI → IL-6	−.01 (.01)	(−.025, .014)	−.01 (.01)	(−.024, .007)	.003 (.01)	(−.018, .018)
TNF-α						
Emotional abuse → BMI → TNF-α	−.005 (.003)	(−.010, .001)	−.005 (.003)	(−.011, .0001)	.001 (.001)	(−.0004, .003)
Physical abuse → BMI → TNF-α	−.0001 (.004)	(−.008, .008)	−.001 (.004)	(−.010, .008)	.001 (.002)	(−.002, .004)
Sexual abuse → BMI → TNF-α	−.004 (.002)	(−.008, −.001)[a]	−.005 (.002)	(−.009, −.0004)[a]	.0004 (.001)	(−.0004, .003)
Emotional neglect → BMI → TNF-α	−.002 (.002)	(−.007, .003)	−.002 (.003)	(−.007, .003)	.0003 (.001)	(−.0004, .002)
Physical neglect → BMI → TNF-α	−.002 (.004)	(−.009, .005)	−.002 (.004)	(−.009, .005)	.0001 (.001)	(−.001, .003)

Note. Effects are reported in unstandardized form. Significant indirect effect findings largely remained when the respective inflammatory marker at each timepoint was used rather than the mean value across pregnancy. CI = Confidence Interval.
[a] Significant effect.

serum CRP were mediated by BMI (Matthews et al., 2014). In the current sample, a similar effect was seen in relation to physical abuse; prepregnancy BMI mediated the relationship between physical abuse and both serum CRP and IL-6 levels. In relation to childhood emotional abuse and neglect with CRP, linear mixed models suggested a similar mediating effect of BMI; however, this was not supported in a more robust PROCESS analysis. Thus, in the current study, a mediating role for prepregnancy BMI was most clearly observed in the context of childhood physical abuse. These findings suggest that interventions targeting maternal obesity may mitigate the effects of childhood trauma on perinatal health.

This study focused on childhood, rather than adult trauma. Childhood is a unique period of vulnerability during which stressor exposure can have long-term effects on physiology (Gunnar & Quevedo, 2007; Miller et al., 2011). A large literature base has shown that early life trauma is associated with dysregulation of the HPA axis (De Bellis & Zisk, 2014; Ehlert, 2013; Gunnar & Quevedo, 2007). Altered levels of corticotropin-releasing factor (CRF), adrencorticotropin levels (ACTH), and cortisol have been found in both observational and experimental studies of youth and adults, with data suggesting early trauma exposure affects long-term baseline functioning of the HPA axis as well as responsiveness to subsequent stressors (De Bellis & Zisk, 2014; Ehlert, 2013; Gunnar & Quevedo, 2007). Exposure to early life trauma may also contribute to epigenetic changes resulting in altered glucocorticoid receptor functioning (De Bellis & Zisk, 2014; Ehlert, 2013; Heim, Newport, Mletzko, Miller, & Nemeroff, 2008). Glucocorticoids play a critical role in regulating inflammation, and the bidirectional relationship between these systems likely sustains dysregulated patterns of functioning (Baumeister et al., 2016; Elenkov & Chrousos, 2002). Thus, HPA dysregulation presents one pathway by which childhood trauma may contribute directly to inflammatory status.

In addition to directly promoting inflammation, such physiological processes have implications for obesity risk. In both animal and human models, administration of glucocorticoids or corticotropin-releasing hormone (CRH) increases consumption of calorie intake compared with those in control groups (Dallman, Pecoraro, & la Fleur, 2005; George, Khan, Briggs, & Abelson, 2010; Tataranni et al., 1996). Similarly, substantial evidence shows an increased likelihood to select as well as consume foods high in fat or sugar in adults exposed to experimentally induced stress (Dallman, 2010; Garg, Wansink, & Inman, 2007; Oliver, Wardle, & Gibson, 2000; Rutters, Nieuwenhuizen, Lemmens, Born, & Westerterp-Plantenga, 2009; Zellner et al., 2006). Childhood trauma exposure also affects disordered eating and poorer sleep quality, both factors which confer obesity risk (Gelaye et al., 2015; Gustafson & Sarwer, 2004). Thus, childhood trauma may contribute to adult inflammatory status via both neuroendocrine dysregulation and behavioral pathways.

The significant findings in the current study with physical abuse in particular may be meaningful. Two studies with large cohorts (≥326 women) found a link childhood physical abuse and prepregnancy obesity (Nagl et al., 2016; Ranchod et al., 2016). For example, examination of 2,873 women showed that prior physical abuse was associated with a 60% increased risk of prepregnancy obesity (Ranchod et al., 2016). Of note, mediation analyses in the current study suggest that the relationship between physical abuse and inflammation is best described as indirect via prepregnancy BMI versus direct. This suggests that the inclusion of obesity status is crucial in determining effective clinical interventions as well as examining future research models with physical abuse and inflammation. The associations between other types of childhood trauma and obesity status are mixed in the literature, with some data showing that relationships between emotional and sexual abuse with prepregnancy obesity did not emerge (Mamun et al., 2007; Nagl et al., 2016). This is consistent with the current study findings showing that while emotional abuse and neglect were directly associated with CRP, these effects were not mediated by prepregnancy BMI. In addition, these associations did not appear to dissipate when covariates (e.g., smoking, medical conditions, depressives symptoms), which could serve as other mediators, were included in the models. The reason for this remains unclear. It is possible that other behavioral pathways, such as emotion regulation strategies, sleep, or other types of affect (e.g., anger, anxiety), are more relevant in explaining the observed effects of emotional trauma on inflammation. Replication of these findings and examination of differential behavioral pathways in the relationship between childhood trauma types and inflammation may address remaining questions.

As described, childhood trauma was not associated with TNF-α in the current study. In addition, no effects of sexual abuse or physical neglect were observed in relation to CRP or IL-6. This study provided longitudinal data in a cohort with high rates of childhood trauma exposure. However, additional associations may emerge within a larger cohort, particularly for types of trauma with relatively low rates of occurrence. For example, sexual abuse affects an estimated 0.5% of children in the US (Finkelhor et al., 2013). Although 23% of women in this sample reported sexual abuse, this was the most infrequent type of trauma reported. Thus, effects of other types of trauma and neglect, including their relation to TNF-α, cannot necessarily be ruled out based on the current data.

The current study relied on retrospective self-reports of childhood trauma, as is common in this literature. Trauma exposure as determined by the CTQ has convergent validity with interview ratings as well as therapist ratings of abuse (D. P. Bernstein et al., 1994; D. P Bernstein et al., 2003; Walker et al., 1999). However, it is possible that the delayed responses or response bias affected these findings. In addition, this study did not examine protective mechanisms (e.g., social support, emotion regulation) which may affect the ultimate health impact of trauma exposure (Hopfinger, Berking, Bockting, & Ebert, 2016; Miller et al., 2011; Stevens et al., 2013). Consideration of these factors would provide a more nuanced understanding of vulnerability and resilience in this context. Finally, the current sample exhibited high CRP levels across pregnancy (raw medians ranged from 6.4 to 8.8) compared with other samples of nonpregnant women (Belo et al., 2005; Maguire et al., 2015; Sacks, Seyani, Lavery, & Trew, 2004). Although the 75th percentile of the interquartile range (IQR; e.g., early pregnancy was 3.0–11.2) is comparable with pregnant women in prior research (Maguire et al., 2015; Picklesimer et al., 2008; Sacks et al., 2004), it is possible that the higher median values in this study are a reflection of specific characteristics of our sample, such as race, income level, and depressive symptoms; as such, these factors should be weighed appropriately when generalizability of the findings is considered.

In sum, these data demonstrate that childhood trauma, particularly emotional abuse, physical abuse, and emotional neglect, is associated with inflammation in pregnant women. In addition, this study provides novel evidence that prepregnancy maternal obesity mediates the association of physical abuse with both serum CRP and IL-6. Thus, addressing maternal obesity prior to pregnancy may in part mitigate negative perinatal health effects of trauma. These findings have relevance for understanding pathways by which early life exposures contribute to perinatal health. Delineation of the role of behavioral mechanisms (e.g., disordered eating) and protective factors (e.g., emotion regulation) in these relationships would be informative.

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