Childhood sexual abuse and IL6 mediated by change in BMI over an 18-year period: A growth curve model

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ABSTRACT

Background: Childhood sexual abuse can increase both body weight and inflammation later in life. Higher weight or faster changes in weight, as measured by changes in body mass index (BMI), may mediate the relationship between childhood sexual abuse and inflammation, however, most studies to date have used a cross-sectional design limiting causal inferences.

Objective: The current study aimed to investigate the interrelationships between childhood sexual abuse, BMI, and C-reactive protein (CRP) and interleukin-6 (IL6).

Participants and Setting.
Data from 461 adults who participated in the Midlife in the United States (MIDUS) study were utilized.

Methods: Growth curve modeling was used to test initial levels of BMI and changes of BMI over an 18-year period as mediators linking childhood sexual abuse to CRP and IL6.

Results: Sexual abuse was not significantly associated with the initial level of BMI; however, sexual abuse was associated with the slope of BMI (b = 0.072, p = .006). BMI intercept (b = 0.080, p = .001) and slope (b = 0.240, p = .002) predicted IL6 values whereas the slope of BMI (b = 0.398, p = .033) but not intercept predicted CRP values. The indirect effect from sexual abuse to IL6 through BMI slope was significant (b = 0.017, 95 % [CI.001, 0.033]) while the indirect effect from sexual abuse to CRP through BMI slope was not significant (b = 0.028, 95 % [CI -0.004, 0.061]).

Conclusion: Childhood sexual abuse was indirectly associated with IL6 through rates of change in BMI over time.

1. Introduction

Childhood maltreatment has been consistently linked to inflammation throughout adulthood (see Coelho, Viola, Walss-Bass, Brietzke, & Grassi-Oliveira, 2014; Kerr, McDonald, & Minnis, 2021 for reviews). This is of critical importance in understanding health aging (e.g., inflammaging) as inflammatory biomarkers are noted risk factors for cardiovascular disease, the leading cause of death in the United States (Franceschi & Campisi, 2014). Indeed, chronic inflammation-related diseases are associated with over 50 % of deaths worldwide, underscoring the paramount role inflammation plays in morbidity and mortality (Furman et al., 2019; Roth et al., 2018). Given the observed age-related increase in inflammation, (Chung et al., 2019) it is imperative to understand underlying factors contributing to this phenomenon.

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The Biological Embedding of Childhood Adversity Model posits that early life adversity and psychological stress can become biologically embedded leading to epigenetic and physiological changes that result in chronic, low-grade inflammation (Miller, Chen, & Parker, 2011). It has been suggested that over 10% of low-grade inflammation is attributed to childhood maltreatment (Danese, Pariente, Caspi, Taylor, & Poulton, 2007). Specifically, childhood maltreatment is positively associated with individual inflammatory biomarkers, such as interleukin-6 (IL6) and C-reactive protein (CRP) (Baldwin et al., 2018; Coelho et al., 2014; Danese et al., 2007; Kerr et al., 2021; Osborn & Widom, 2020). Additionally, obesity is associated with both childhood maltreatment, particularly sexual abuse, and the elevation of inflammatory markers and may serve as a mediator connecting the two (Schroeder, Schuler, Kobulsy, & Sarwer, 2021).

1.1. Theoretical background

The Biological Embedding of Childhood Adversity Model (BECAM) is a biopsychosocial model that provides a theoretical framework for understanding how childhood maltreatment is connected to inflammation in adulthood. According to the BECAM model, early life adversity becomes biologically embedded in the body through physiological processes that lead to systemic inflammation (Miller et al., 2011). Experiencing consistent adversity during this time remolds the nervous system via alterations in the synaptic connections and neural development (McLaughlin, Weissman, & Bitran, 2019). Repeated childhood adversity has epigenetic consequences such as modification of gene expression and posttranslational modifications. Together, these epigenetic and physiological changes potentiate physiological systems to increase proinflammatory cytokines leading to chronic, low-grade inflammation (Miller et al., 2011). Likewise, childhood adversity has been linked to a blunted cortisol response, which is an anti-inflammatory hormone (Schräf, Mürner-Lavanchy, Schmidt, Koenig, & Kaess, 2022). The combination of greater pro-inflammatory cytokines combined with blunted anti-inflammatory hormones leaves the body in a prolonged state of inflammation manifesting in higher levels of interleukin-6 (IL6) and C-reactive protein (CRP) across the life course.

Another proposition of the BECAM is that childhood maltreatment impinges on psychosocial development that increases risk for inflammation (Miller et al., 2011). Children who experienced adversity often struggle with developing social skills, healthy relationships, and effective coping strategies (Hamstra & Fitzgerald, 2021). Childhood adversity fosters vigilance to threat, mistrust of others, negative beliefs about people and relationships, and negative appraisals of ambiguous social situations (Miller et al., 2011). Thus, those with a history of adversity tend to have more conflictual relationships, experience more rejection and isolation, and have less positive, supportive relationships (Miller et al., 2011; Shahab et al., 2021). The impacts of childhood maltreatment on physiological and psychosocial development can present challenges in successfully fulfilling social roles (i.e., education and job related responsibilities) throughout life, which can lead to fewer resources (i.e., lower paying jobs, less access to and lower quality healthcare, fewer benefits), lower health literacy (i.e., utilizing healthcare resources, seeking out preventative care), and less effective coping (i.e., more health hindering behaviors and less health protective behaviors) which are known to influence inflammation and inflammatory diseases (Braveman & Gottlieb, 2014; Hyvert et al., 2023; Lodi-Smith et al., 2010; Miller et al., 2011; Raposa, Bower, Hammen, Najman, & Brennan, 2014; Stormacq, van den Broucke, & Wosinski, 2019; Tormey et al., 2019; Zajacova & Lawrence, 2018; Zilioli, Imani, & Slatcher, 2017).

1.2. Childhood maltreatment and inflammation

Childhood maltreatment occurs in the first 17 years of life and is one of the most common forms of childhood adversity and consists of physical, emotional, and sexual abuse, and physical and emotional neglect. Experiences of childhood maltreatment are common with prevalences ranging from 8%–36.5% for subtypes of maltreatment in North America (Stoltenborgh, Bakermans-Kranenburg, Alink, & van Uzendoorn, M. H., 2015). Researchers have consistently found that maltreatment is linked to systemic inflammation in adulthood using both prospective and retrospective reports of maltreatment (see Coelho et al., 2014 for review). Moreover, studies have shown that childhood maltreatment is positively associated with individual inflammatory biomarkers, most commonly, interleukin-6 (IL6) and C-reactive protein (CRP) (Baldwin et al., 2018; Coelho et al., 2014; Danese et al., 2007; Kerr et al., 2021; Osborn & Widom, 2020). While maltreatment consists of several subtypes of both abuse and neglect, sexual abuse is a particularly insidious form of maltreatment that may have especially strong effects on inflammation. Indeed, childhood sexual abuse is consistently associated with increases in inflammatory biomarkers (Bertone-Johnson, Whitcomb, Missmer, Karlson, & Rich-Edwards, 2012; D’Elia et al., 2018; Ghosh et al., 2018; Matthews, Chang, Thurston, & Bromberger, 2014; Quagliato & Nardi, 2023) and demonstrates significant associations with risk factors for inflammation, notably BMI (Danese & Tan, 2014).

1.3. Childhood sexual abuse, BMI, and inflammation

Childhood sexual abuse has long been associated with adult obesity, regardless of study design, measure, and definitions used (Rohde et al., 2008; Schroeder et al., 2021). Finkelhor and Browne (1985) proffer that childhood sexual abuse is characterized to sexual traumatization, stigmatization, powerlessness, and guilty. As a consequence of being sexually objectified, clinical knowledge suggests that gaining weight is a protective mechanism from future victimization (van der Kolk, 2014). Wiss, Brewerton, and Tomiyama (2022) proffered that sexual abuse becomes biologically embedded, triggering a cascade of physiological effects (e.g., inflammation) that contribute to food addiction, eating disorders, and emotional eating that contributes to greater BMI. Chronic stress can lead to an increase in the food-associated drive and desire to consume “comfort foods” to mitigate the stress response (Dallman, Pecoraro, & la Fleur, 2005) which can offer short term regulation but may lead to long term consequences due to a positive energy
balance (Kazmierski, Borelli, & Rao, 2022). These associations may be especially important for victims of sexual abuse due to increased relative risk of overeating and weight and shape concern (Emery, Yoon, Mason, & Neumark-Sztainer, 2021). Not surprisingly, studies have found that sexual abuse in childhood is linked to higher BMI and obesity in adulthood (Gustafson & Sarwer, 2004; Offer et al., 2022). Overall, the association between abuse and BMI differs by age, with a greater impact as adults move through the life course, indicating a need to consider a life course perspective that assesses both cross sectional BMI and changes over time (Danese & Tan, 2014; Oh et al., 2018; Power, Pinto Pereira, & Li, 2015; Schroeder et al., 2021; Shin & Miller, 2012).

The prevalence of obesity, as defined by a BMI over 30, is increasing rapidly with recent reports suggesting that 39.8% of adults in the United States are obese with the highest prevalence among middle aged adults (Hales, Carroll, Fryar, & Ogden, 2017). Obesity is associated with adverse consequences on physical health and psychosocial functioning (Chooi, Ding, & Magkos, 2019; Wyatt, Winters, & Dubbert, 2006) such as an increase in fat mass, or adipose tissue. Adipose tissue produces a variety of pro-inflammatory markers, such as IL6, which signals a cascading effect including the production of other inflammatory markers such as CRP (see Ellulu, Patimah, Khaza’ai, Rahmat, & Abed, 2017 for review). In fact, a study of morbidly obese patients showed significantly lower levels of IL6 and CRP 12 months after bariatric surgery suggesting a direct and reversible impact between BMI and inflammatory markers (Ilían-Gómez et al., 2012). Although this clinical sample may not represent the general population, the direct effect of decreased BMI on inflammatory markers supports BMI as a potential mediator between childhood sexual abuse and inflammation during adulthood. This has been supported in a longitudinal study of midlife women which found that elevated BMI significantly influenced the relationship between childhood sexual abuse and CRP 7 years later (Matthews et al., 2014).

1.4. Limitations of current research

Existing research has several methodological limitations and addressing them would enhance current knowledge and strengthen conclusions. Sexual abuse has been demonstrated to be linked to increased biomarker levels at different time points throughout the life course, but studies have yet to utilize longitudinal measures connecting sexual abuse to inflammation over time. For example, cross-sectional studies have linked childhood maltreatment to increased inflammation in young adults, midlife adults, and older adults (Coelho et al., 2014; Kerr et al., 2021), however, to our knowledge, the longitudinal impact of childhood maltreatment on inflammation has been seldom studied in adults. One study conducted by Renna et al. (2021) found that a history of childhood maltreatment predicted steeper increases in inflammation over time but did not explicitly test rates of growth or identify mediators. A second notable limitation is that some studies only included one inflammatory biomarker without considering others (Baldwin et al., 2018; Coelho et al., 2014; Entringer et al., 2020; Kerr et al., 2021; Osborn & Widom, 2020), which precludes a complete picture of systemic inflammation. Third, several studies failed to consider the impact of BMI on inflammation, a factor that is known to have a strong influence on IL6 and CRP (Coelho et al., 2014; Kerr et al., 2021; Palmos et al., 2019).

Finally, the use of non-linear transformation (e.g., log transformations) of inflammatory biomarkers poses a significant threat to validity (Changyong et al., 2014). Historically, the use of non-linear transformation was required to appropriately analyze non-normal data; however, recent advances address non-normality without data manipulation. The first problem is that non-linear transformations can impugn construct validity via a lack of substantive concern for theoretical implications for altering the nature of the transformed variable. Stated another way, it is unclear what log CRP and IL6 scores theoretically represent. Of consequence, a chasm between the hypothesis and the analytic procedures is created (Becker, Robertson, & Vandenberg, 2019). Non-linear transformations fundamentally change the characteristics of the distribution (e.g., skewness, kurtosis, density), which inserts substantive uncertainty into the meaning of the transformed scores and associations with other variables, thus non-linear transformations can increase the risk for Type II error. Third, the use of non-linear transformations decreases external validity because the distributions of transformed variables may not occur in the real world, suggesting that the associations among the examined variables do not occur in the population while potentially masking relationships that do (Becker et al., 2019). Finally, log transformations are often used to transform skewed data but often increases skewness (Feng, Wang, Lu, & Tu, 2013).

1.5. Present study

The purpose of the current study was to investigate the interrelationships between sexual abuse, changes in BMI, and CRP and IL6. To address the gaps mentioned above, we use growth curve modeling to test initial levels of BMI and change of BMI over an 18-year period as mediators linking childhood sexual abuse to CRP and IL6. First (H1), we hypothesized that sexual abuse will be positively associated with higher starting levels of BMI and greater increases in BMI over time. Second (H2), we hypothesized that the rates of change in BMI, but not initial status, will be positively associated with both IL6 and CRP. Third (H3), we hypothesized indirect effects between sexual abuse and both IL6 and CRP through increases in BMI will be significant.

2. Method

2.1. Participants and procedure

Data for the current study are from the Midlife in United States (MIDUS) study. IRB was not required for the current study since MIDUS data are free, de-identified, and publicly available (https://www.icpsr.umich.edu/web/ICPSR/series/203). The MIDUS study includes matched, multiple wave data collected from 1995–1996 (MIDUS 1), 2004–2006 (MIDUS 2), and 2014–2016 (MIDUS 3). Telephone interviews, self-administered questionnaires, and in-person data collection provide data on psychosocial constructs, self-
reported physical morbidity, biomarker data, behavioral measures, and social factors. The MIDUS 1 sample comprised of 7108 individuals from a national random digit dialing sample, city oversamples, sibling data, and twin data. Following MIDUS 2 (N = 1255) and MIDUS 3 (N = 787), a subset of participants participated in biological data collection. For attritional analyses across the MIDUS study see papers by Radler and colleagues (Radler & Ryff, 2010; Song et al., 2021).

The study’s primary variables were extracted from a sample of adults (n = 461) that participated in MIDUS 2, MIDUS 3, MIDUS 2 biomarker study (2005–2009) and MIDUS 3 biomarker study (2017–2022) and were not a part of the twin or sibling subsample; one twin/sibling was randomly removed to avoid violation of independence of residuals, resulting in biased standard errors. Several covariates were extracted from MIDUS 2. The average lag in time between the MIDUS 2 and MIDUS 3 biomarker study was approximately 12 years (due in part to COVID-19). The study sample was predominantly female (52.5 %) and White (90.0 %), and the mean age was \( M = 43.64 \) (SD = 10.04) at MIDUS 1.

2.2. Measures

**Sexual Abuse.** Childhood sexual abuse was assessed using the childhood trauma questionnaire (CTQ; Bernstein et al., 2003). The CTQ is a 25-item scale that was used to measure childhood abuse and neglect prior to the age of 18. Items are scored on a five-point Likert scale, ranging from (1) ‘Never’ to (5) ‘Very Frequently.’ An example of sexual abuse item was “Someone molested me.” We examined subscales separately; sexual abuse was determined with a sum of 0–25. Higher scores reflect greater severity of maltreatment. The CTQ has been found to have construct validity and criterion-related validity (Bernstein et al., 2003) and the Cronbach’s alpha = 0.93.

**Body Mass Index.** BMI was calculated as weight in kilograms (kg) divided by the square of height in meters (m). This was based on self-report data collected at MIDUS 1, 2, and 3. For adults, BMI less than 18.5 is underweight, 18.5–24.9 is healthy, 25–29.9 is overweight, and 30 or higher is obese (National Heart, Lung, Blood Institute, National Institute of Diabetes, Digestive, & Kidney Diseases, 1998).

**Inflammatory Biomarkers.** Inflammatory biomarkers were assessed with two common indicators of inflammation: IL6 and CRP. The biomarkers IL6 and CRP were obtained from blood samples the morning after a 12 h fast which occurred during the participant’s overnight stay at one of three clinical labs (UCLA, Madison, Georgetown). IL6 concentrations were measured using blood serum and enzyme linked immunosorbent assay (ELISA) and CRP concentrations were measured using blood plasma and immunonephelometry. The biomarker values were not log-transformed and robust statistical methods to non-normality were employed (see statistical analysis section), so that external validity is not threatened due to a non-linear statistical manipulation.

2.3. Covariates

**Subtypes of Childhood Maltreatment.** Emotional and physical abuse and neglect were also assessed using the childhood trauma questionnaire, see overview above (CTQ; Bernstein et al., 2003). Additional details are provided in the online supplementary material.

**Age.** Participants’ age was entered as a continuous variable.

**Race.** Due to the sample being substantially White, we dichotomized race into 0 = racial minority, 1 = White.

**Education.** Educational achievement was measured with one item and responses ranged from 1 = No school/Some grade school to 12 = PhD /Ed.D/M.D., J.D.

**Anti-Inflammatory Medication Use.** Anti-inflammatory medication use was dichotomized based on participants’ self-report of use of any nonsteroidal anti-inflammatory drugs (NSAID) with yes = 1 and no = 0.

**Eating Habits.** The MIDUS Healthy Eating Index was used to determine eating habits, which is calculated based on the amount of vegetables and fruits, whole grains, oily fish, lean meat, non-meat protein, sugared beverages, high fat meat, fast food, fermented dairy, and alcohol consumed on a regular basis. Higher scores reflect healthier eating habits. A change score was created by subtracting the score from the Healthy Eating Index at time three and time two. Alcohol consumption was included in the eating habit variables and was therefore not assessed as a separate variable.

**Sleep.** The Pittsburgh Sleep Quality Index (PSQI) (Buysse, Reynolds III, Monk, Berman, & Kupfer, 1989) is a self-administered questionnaire used to assess participants’ sleep quality. A global score between 0 and 21 is used with higher scores indicating more sleep problems. A change score was created to assess changes in sleeping habits between time point three and time point two. Cronbach’s alpha = 0.69.

**Exercise.** Exercise was dichotomized based on the answer to the following question “do you engage in regular exercise, or activity, of any type for 20 minutes or more at least 3 times/week?” with yes = 1 and no = 0.

2.4. Statistical analysis

To examine the interrelationships between sexual abuse, body mass index, and CRP and IL6, we conducted a multistage analytic process. First, we scanned our data for outliers and influential observations. Specifically, we used clinical guidelines set for healthy individuals in the general population to determine whether there were outliers in any of the main study variables (BMI, IL6, CRP). We removed one person with an extremely high IL6 value at MIDUS 3 from our study sample, because values outside of the defined range of IL6 in healthy individuals reflect an acute inflammatory response to infections or diseases (Said et al., 2021). Second, descriptive statistics were run, including bivariate correlations, means, and standard deviations among the study constructs.

Third, we used structural equation modeling to investigate the primary aims. We first fit an unconditional growth model estimating...
Table 1
Bivariate Correlations, Means, and Standard Deviations of Independent, Mediating, Outcome, and Control Variables.

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BMI: body mass index; CRP: C-reactive protein; IL6 interlukein-6.

*p < .05. **p < .001.
the latent intercept and slope of BMI over the three waves. The intercept latent variable has factor loadings fixed to 1 for each of the BMI indicators and the slope factor loadings were fixed to 1, 2, and 3 for BMI at MIDUS 1, 2, and 3 respectively. The intercept latent factor is interpreted as the mean value of BMI at time 1 and the slope latent factor is the rate of change in BMI over time. The intercept and slope each have mean components (e.g., are the intercept and slope estimates different than zero) and variance components (e.g., do individuals significantly differ in levels of BMI at time 1 or rates of change, respectively). Following the unconditional growth model, we included time invariant covariates (race, age, education, and baseline IL6 and CRP, anti-inflammatory medication use, changes in eating habits, changes in sleeping quality, and exercise) and the independent, and outcome variables into the model (e.g., conditional growth model). Additionally, we had the intercept predict the slope because we would expect that the higher levels of BMI at time 1 would be associated with lower increases in BMI over time. We used maximum likelihood with Satorra-Bentler chi-square adjustment (MLR), which is robust to non-normality (Muthén & Muthén, 1998–2007; Satorra & Bentler, 2001), and while it precludes estimation of bootstrapping, it provides similar estimates. To estimate indirect effects, we estimated a point estimate and 95% confidence intervals. Several fit statistics were used to evaluate the model-data fit including the comparative fit index (CFI), root mean square error of approximation (RMSEA), standardized root mean square residual (SRMR), and the chi-square test ($\chi^2$). The CFI indicates acceptable fit above 0.90 and demonstrate good fit above 0.95. RMSEA demonstrates acceptable fit below 0.08 and good fit below 0.05 (Hu & Bentler, 1999). A non-significant chi-square statistic demonstrates strong model-data fit but is rarely achieved in practice as it is an overpowered statistic (Little, 2013). Additionally, we examined the residual covariance matrix to identify possible local misfit (e.g., over or under estimation of model expected means, variances, and covariances).

To handle missing data, we employed full information maximum likelihood estimation (FIML; Enders, 2023). FIML is the default estimator in Mplus and assumes that data are either missing completely at random (MCAR) or missing at random (MAR). MCAR occurs when there are not systematic patterns and values while MAR have patterns of missing data, but the patterns are correlated with (explained by) variables within the data that can be added to the model as auxiliary variables. The inclusion of auxiliary variables in the prediction of missingness increases statistical power, addresses non-response bias, adjusts standard errors, and provides more accurate test statistics (Baraldi & Enders, 2010; Enders, 2008, 2023). Further, auxiliary variables are effective even when there is a considerable amount of missing data (over 30%) (Baraldi & Enders, 2010). Regarding the current study, missing data were not greater than 15% for any pair of variables and was largely due to missing BMI measurements. We specified the following as auxiliary variables: number of chronic conditions at MIDUS 2 and MIDUS 3, and depression at MIDUS 1.

### 3. Results

#### 3.1. Bivariate results

The correlations, means, and standard deviations for all variables can be seen in Table 1.

#### 3.2. Unconditional growth model

First, an unconditional growth model was examined to determine if there are indeed changes in BMI over time. The unconditional growth model included time invariant covariates and the independent and outcome variables. The fit statistics indicated good fit with CFI = 0.95, RMSEA = 0.04, and SRMR = 0.03. The beta coefficients for the intercept and slope were 0.7 and -0.3, respectively, indicating a significant increase in BMI over time.

![Fig. 1. Results from the growth curve model examining BMI as a mediator linking childhood sexual abuse to IL6 and CRP.](image-url)
growth model demonstrated good model-data fit: \( \chi^2 (1) = 22.781, p < .001, \text{CFI} = 0.94, \text{RMSEA} = 0.08, \text{SRMR} = 0.08; \) we found no evidence that there were substantial modifications in the residual covariance matrix that would yield different substantive conclusions. The intercept of was significantly different from 0 \( (M = 26.24, p < .001) \) as was the slope \( (M = 0.98, p < .001) \). The positive slope indicates that there was a significant, upward trend in BMI over the course of adulthood. Also within the unconditional growth model is variation within the slopes and intercepts. There was significant variation in the intercepts \( (s^2 = 22.32, p < .001) \) and slopes \( (s^2 = 2.75, p = .005) \), suggesting that adults varied both in terms of initial levels of BMI as well as rates of change in BMI over the 18-year period.

### 3.3. Conditional growth curve model

Next, as shown in Fig. 1, we estimated the conditional growth model and the model-data fit for the growth curve model demonstrated adequate fit: \( \chi^2 (29) = 56.22, p = .002, \text{CFI} = 0.97, \text{RMSEA} = 0.05, \text{SRMR} = 0.05. \) Sexual abuse was not significantly associated with the initial level of BMI \( (b = 0.071, SE = 0.102, p = .488) \), however, sexual abuse was associated with the slope of BMI \( (b = 0.072, SE = 0.026, p = .006) \) suggesting a higher report of childhood sexual abuse resulted in a larger increase in BMI over time. The intercept of BMI inversely predicted the slope of BMI \( (b = -0.134, SE = 0.050, p = .008) \) indicating that individuals who had higher BMIs at time point one had a slower rate of change over time.

BMI intercept \( (b = 0.080, SE = 0.023, p = .001) \) and slope \( (b = 0.240, SE = 0.078, p = .002) \) predicted IL6 values whereas the slope of BMI \( (b = 0.398, SE = 0.186, p = .033) \) but not intercept \( (b = 0.095, SE = 0.053, p = .074) \) predicted CRP values. This suggests that higher BMI at time point one predicts IL6 values in midlife adults, and a faster rate of change in BMI over time predicts both IL6 and CRP. Sexual abuse did not predict IL6 \( (b = -0.019, SE = 0.027, p = .469) \) or CRP \( (b = -0.034, SE = 0.071, p = .627) \). The indirect effect from sexual abuse to IL6 through BMI slope was significant \( (b = 0.017, 95\% [CI0.01, 0.033]) \). The indirect effect from sexual abuse to CRP through BMI slope was not significant \( (b = 0.028, 95\% [CI -0.004, 0.061]) \). We had expected to include gender as a covariate but were unable to do so due to a non-positive definite first order derivative product matrix, which is indicative of a small or 0 determinants indicating multicollinearity. Parameter estimates of the covariates can be seen in the online supplementary material.

### 4. Discussion

It is widely known that childhood maltreatment is linked with health problems in adulthood (Grummitt et al., 2021), and more recently, research has begun to focus on identifying specific mechanisms through which adversity impacts the functioning of physiological systems. The current study tested the indirect effect of BMI linking childhood sexual abuse on CRP and IL6. We found that childhood sexual abuse was indirectly associated with IL6 through rates of change in BMI over time. Indirect effects between sexual abuse and CRP through BMI slopes and intercept were not significant.

The study makes several significant contributions to the literature. The current study found that those who reported more severe sexual abuse also experienced greater increases in BMI, partially supporting our first hypothesis (H1). Sexual abuse has been demonstrated to be associated with increased BMI (Hemmingsson, Johansson, & Reynisdottir, 2014; Schroeder et al., 2021). Sexual abuse survivors often develop unhealthy eating patterns such as binge eating and overeating tendencies (Yoon, Emery, Mason, & Neumark-Sztainer, 2012), which may be a way to cope with the traumatic experiences of sexual abuse. As a manifestation of internalized shame that often accompanies sexual abuse victimization (MacGinley, Breckenridge, Neumark-Sztainer, 2021), which may be a way to avoid attracting the attention of others, and protect themselves from revictimization and retraumatization by hiding behind a physical appearance that is generally viewed as less desirable in Western cultures (Brewis, SturtzSoretharan, & Wutich, 2018; Richmond, Austin, Walls, & Subramanian, 2012).

Our findings indicated that more rapid increases in BMI predicted increases in both IL6 and CRP suggesting that faster rates of weight gain over time lead to an increase in both biomarkers, supporting our second hypothesis (H2). This is consistent with previous research showing that increases in adipose tissue result in the upregulation of pro-inflammatory cytokine production (Ellulu et al., 2017; Fogarty et al., 2008). We utilized repeated measures of inflammation over a nine-year period, and thus, addressed prior levels of inflammation. Inflammation tends to increase with age (Chung et al., 2019), and it is imperative to account for previous levels of inflammation to accurately examine mechanisms that may increase inflammation over time.

Interestingly, the positive association between the intercept of BMI and IL6 remained significant after accounting for covariates, but was not significant for CRP. This is important, because this finding suggests that previous levels of BMI are a strong determinant of future trajectories of IL6, and the upregulation of pro-inflammatory processes related to increased white adipose tissue may persist over time. IL6 and CRP production happen at different points of inflammatory processes: IL6 plays a role in mediating and coordinating inflammatory responses and is more directly impacted by adipose tissue, whereas CRP is produced as a result of a proinflammatory cascade stimulated by IL6 (Del Giudice & Gangestad, 2018; Ellulu et al., 2017). Therefore, it may be that while IL6 production remains higher, subsequent inflammatory processes lessen or dissipate. Many studies only focus on one inflammatory biomarker and cannot demonstrate potential differences in how different inflammatory biomarkers are impacted by abuse and subsequent mediating pathways (Baldwin et al., 2018; Coelho et al., 2014; Kerr et al., 2021; Osborn & Widom, 2020).

The present study demonstrated that the indirect effect between sexual abuse and IL6 through BMI slope was significant, partially supporting our third hypothesis (H3). This finding supports previous research suggesting that BMI is a mediator linking sexual abuse to inflammation (Matthews et al., 2014). This is a particularly notable contribution in the context of sexual abuse, as there is a dearth of longitudinal biomarker research. Previous research studying relationships between childhood maltreatment and inflammatory outcomes either failed to consider the contributions of BMI to inflammation or accounted for the influence of BMI at one time point only (Coelho et al., 2014; Kerr et al., 2021; Palmos et al., 2019), therefore, our findings advance the knowledge on the longitudinal impacts...
of changes in BMI on inflammation.

On the other hand, changes in BMI were not a significant mediator between sexual abuse and CRP, although the direct effects were both significant. This finding is inconsistent with previous research. In a 7-year longitudinal study of women, Matthews and colleagues found that percent annual change in BMI mediated the relationship between childhood sexual abuse and CRP, however, the authors did not control for prior levels of CRP (Matthews et al., 2014). The role of CRP in inflammatory processes has been debated by researchers and appears to be complex. There are two isoforms of CRP, one pro-inflammatory and one anti-inflammatory (Del Giudice & Gangestad, 2018). These isoforms differ in solubility and therefore differences in plasma or saliva samples may reflect variations in isoforms (Trial, Potempa, & Entman, 2016). The current study measured CRP through plasma levels. Although large increases in plasma CRP can indicate reparatory processes employed as a response to inflammation, generally, plasma CRP is an indicator of somatic maintenance mechanisms and does not directly reflect inflammation (Del Giudice & Gangestad, 2018). Thus, our finding that higher rates of change in BMI necessitate increases in anti-inflammatory and somatic maintenance processes but do not mediate the relationship between sexual abuse and anti-inflammatory processes appear to be consistent with the physiological mechanisms of inflammation. Regardless, our results and prior research suggest that interventions that aim to support a healthy BMI may have small, but impactful changes in CRP which can have profound implications for individuals’ health outcomes.

The last notable contribution of our study is that we did not log-transform IL6 and CRP values. Although historically non-linear transformation has been frequently used in biomarker research due to the non-normality of distributions, this can introduce threats to validity (Becker et al., 2019). Thus, replicating findings of previous research regarding the relationships between sexual abuse, BMI, and inflammation using non-transformed data is crucial in understanding the true nature of these relationships. Our findings increase confidence that the associations are valid among childhood maltreatment, BMI, and inflammation over time.

5. Limitations and future directions

Although the study makes several significant contributions, there are limitations that future research should address. First, our sample primarily consisted of White middle-class adults, and results may not be generalizable to racial minorities and people of lower socioeconomic status. Previous research has noted that individuals of different racial and socioeconomic groups have varying inflammatory profiles (Paalani, Lee, Haddad, & Tonstad, 2011; Schmeer & Tarrence, 2018). Future research should investigate whether our findings can be extended to more diverse groups. Second, we were unable to add gender into our model due to inadmissible solutions. Sexual abuse is reported at higher rates by women compared to men (Gustafson & Sarwer, 2004) and prior research found gender differences in the impact of childhood sexual abuse on BMI over time (Power et al., 2015), so future research should endeavor to identify possible nuances. Third, while examining changes in BMI and inflammation over nine-year periods is a considerable advancement to the current literature, there may be more nuanced changes in inflammation over shorter periods of time and it may be valuable to take more frequent repeated measures of both BMI and inflammatory biomarkers. Fourth, we used retrospective reports of maltreatment. Using prospective and multi-informant reports would be beneficial in replicating and substantiating the findings. Lastly, emotional neglect demonstrated a significant inverse association with BMI in adulthood and may be a notable area to explore in the future.

Future research should focus on successful methods to promote healthy eating habits and behaviors for survivors of childhood sexual abuse. Reducing the risk of overeating, emotional eating, eating disorders, and other unhealthy behaviors may not only promote healthy weight during early adulthood, but also mitigate the risk of inflammation and related outcomes in later adulthood. Chronic inflammation-related diseases are a contributor to many of the leading causes of death globally; therefore, interventions that encourage healthy eating behaviors and healthy weight may drastically impact health across the lifespan, especially for survivors of childhood sexual abuse.

6. Conclusion

To our knowledge, this is the first study to examine rates of change in BMI over time as a mediator between sexual abuse history and inflammatory biomarkers. Rates of change in BMI appear to influence inflammatory outcomes of adult survivors of childhood sexual abuse. Targeting BMI as a point of intervention throughout adulthood may be beneficial in this population. Reducing the rate of change in BMI over time could lead to the prevention and mitigation of inflammatory risks, and thus, morbidity and early mortality.

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CRediT authorship contribution statement

Haley Hall: Writing – review & editing, Writing – original draft, Project administration, Conceptualization. Viktoria Papp:...
Writing – original draft, Conceptualization. **Michael Fitzgerald**: Writing – review & editing, Writing – original draft, Supervision, Methodology, Formal analysis, Conceptualization.

**Declarations of interest**

none

**Data availability**

MIDUS data are free, de-identified, and publicly available

**Appendix A. Supplementary data**

Supplementary data to this article can be found online at https://doi.org/10.1016/j.chiabu.2024.106914.

**References**


