The Interaction of Trauma Exposure and DNA Methylation on Blood Pressure Among Black Women in the InterGEN Study

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ABSTRACT

OBJECTIVE: Despite evidence that trauma exposure is linked to higher risk of hypertension, epigenetic mechanisms (such as DNA methylation) by which trauma potentially influences hypertension risk among Black adults remain understudied.

METHODS: Data from a longitudinal study of Black mothers were used to test the hypothesis that direct childhood trauma (ie, personal exposure) and vicarious trauma (ie, childhood trauma experienced by their children) would interact with DNA methylation to increase blood pressure (BP). Separate linear mixed effects models were fitted at each CpG site with the DNA methylation beta-value and direct and vicarious trauma as predictors and systolic and diastolic BP modeled as dependent variables adjusted for age, cigarette smoking, and body mass index. Interaction terms between DNA methylation beta-values with direct and vicarious trauma were added.

RESULTS: The sample included 244 Black mothers with a mean age of 31.2 years (SD = ±5.8). Approximately 45% of participants reported at least one form of direct childhood trauma and 49% reported at least one form of vicarious trauma. Epigenome-wide interaction analyses found that no CpG sites passed the epigenome-wide significance level indicating the interaction between direct or vicarious trauma with DNAm did not influence systolic or diastolic BP.

CONCLUSIONS: This is one of the first studies to simultaneously examine whether direct or vicarious exposure to trauma interact with DNAm to influence BP. Although findings were null, this study highlights directions for future research that investigates epigenetic mechanisms that may link trauma exposure with hypertension risk in Black women.

KEYWORDS: Blood pressure, childhood trauma, epigenomics, African American, women's health

Introduction

Hypertension, defined as a blood pressure (BP) of 130/80 mmHg or higher, affects approximately 50% of American adults.[1,2] Hypertension is one of the most important and prevalent risk factors for cardiovascular disease (CVD) and the leading cause of death and disability worldwide.[3,4] In the United States (U.S.), the prevalence of hypertension is not equal across racial and ethnic groups with Black adults exhibiting higher rates (57.1%) compared to White adults (43.6%).[2]

Childhood trauma (eg, abuse, neglect, household dysfunction) is a significant public health concern in the U.S. It is estimated that 1 in 7 children have experienced at least one form of childhood trauma in the past year.[5] Childhood trauma has a significant economic burden (eg, healthcare costs, productivity loss, judicial costs) in the U.S. with costs estimated as high as $428 billion in 2015.[6,7] There is growing evidence that childhood trauma is associated with increased risk for hypertension in adulthood.[8-10] For instance, a 2017 systematic review of 24 studies found that childhood trauma was positively associated with hypertension in 60% of included studies.[9] Furthermore, analyses of data from the Nurses' Health Study found that sexual and physical abuse prior to age 18 had a dose-dependent relationship with hypertension.[10]

The prevalence of childhood trauma also differs across racial and ethnic groups in the U.S. The Fourth National Incidence Study of Child Abuse and Neglect Federal Report to Congress indicated that the rate of childhood trauma among Black children was approximately 2 times higher than the rate for Non-Hispanic White children.[11] In addition, recent analyses of data from the National Survey of Children's Health have found that Black children report a higher total number of childhood traumatic experiences relative to their Non-Hispanic White peers.[12-14]

The most often cited explanation for the higher prevalence of childhood trauma observed among Black children is that they are more likely to live in poverty.[12,14] Lower socioeconomic status may increase Black children's vulnerability to the adverse health effects of childhood trauma as children living in poverty often lack adequate social and emotional resources to cope with these experiences.[15] Further, racism—experienced indirectly through the impacts of income inequality on parenting stress or racialized drug enforcement and mass incarceration on family structures as well as directly through interpersonal racism, over-policing, and neighborhood violence—predisposes Black children to childhood trauma.[16,17]

The link between trauma exposure and hypertension is multifactorial and hypothesized to be mediated by psychological, behavioral, and physiological pathways.[15,18]Survivors of childhood trauma are at increased risk of mental health conditions, such as depression, anxiety, and posttraumatic stress disorder (PTSD) [19]; all of which are associated with elevated risk of hypertension.[20] There is evidence that individuals with a history of childhood trauma engage in health risk behaviors (eg, unhealthy diet intake,[21] heavy alcohol consumption,[22] and lifetime cigarette smoking[23]) that confer increased risk of hypertension.[24] Multiple studies indicate that exposure to trauma is associated with dysregulation of several physiological systems that have been shown to influence BP.[25-28] For instance, report of childhood trauma is associated with increased concentrations of circulating catecholamines and pro-inflammatory markers (eg, C-reactive protein, interleukin-6 [IL-6])[18,29-32] as well as epigenetic modifications (eg, DNA methylation [DNAm]).[33]

DNAm has been implicated in the development of chronic conditions among adults, such as hypertension, CVD, and diabetes.[34-38] DNAm is an epigenetic modification that consists of the addition of a methyl group to the C5 position of the cytosine residue, which forms a 5-methylcytosine. DNAm can modify expression of a gene by altering binding of transcription factors to DNA or recruiting proteins involved in gene repression.[39,40] Epigenetic programing has been suggested as a mechanism through which childhood trauma may become "biologically embedded," contributing to negative health outcomes later in life.[41-43] A recent systematic review of 100 studies found that childhood trauma was associated with significant epigenetic modifications across the genome[33]; nineteen of these studies examined epigenome wide associations of childhood trauma in adulthood and only 2 included primarily Black samples.[44,45] Overall, trauma exposure was associated with DNAm of several genes that play a role in regulating hypothalamic-pituitary-adrenal axis function (eg, *NR3C1*, *FKBP5*, *CRHR1*, and *POMC*) and inflammation (eg, *IL-6*),[33] both of which are known to influence BP.[25-28]

Epigenetic mechanisms by which trauma exposure potentially influences the health of Black adults remain understudied. The majority of studies that have examined the influence of childhood trauma on DNAm have been conducted in samples of primarily European or Asian ancestry with only a small number of studies focused on individuals of African ancestry.[33] In a small study of Black men living in Chicago (N = 34), investigators found that a higher self-report of more frequent and severe childhood trauma was associated with lower DNAm of the *IL-6* gene in peripheral blood.[46] In addition, investigators in 3 studies of Black women and men found no association between childhood trauma and the oxytocin-receptor-gene (*OXTR*).[47-49] Although hypertension is a highly prevalent health condition among Black adults, to date, no study has examined epigenetic mechanisms that link trauma exposure with BP in this population.

Although the link between direct exposure to childhood trauma and BP is well-established,[15,18] no study has examined the association of vicarious trauma exposure with hypertension risk. Vicarious trauma exposure can be defined as traumatic experiences that do not directly happen to an individual, but which an individual witnesses, learns about, or hears about from others (eg, friends, family, media coverage).[50-52] Traumatic experiences that occur to one's child may have an impact on a parent's health and wellbeing. Indeed, several studies have shown that non-offending parents who learn that their child has been sexually abused report high levels of psychological distress and depression.[53-55] Research on other adverse health outcomes associated with vicarious trauma experienced by one's child is limited. However, we hypothesize that the stress of learning about or witnessing trauma experienced by one's child can have similar effects on BP as those observed for direct trauma exposure. To date, vicarious trauma has not been tested in prior studies that investigated epigenetic mechanisms that contribute to the association of trauma with BP.

Given that DNAm has been previously associated with trauma exposure and plays a role in hypertension development,[37,38] the goal of the present study was to evaluate the influence of gene-environment interaction (eg, DNAm × direct childhood trauma) on BP in Black women, a population that may be at particularly high risk for both trauma exposure and hypertension. Our analyses were informed by the American Heart Association's model of childhood adversity and cardiometabolic health, which posits that greater exposure to traumatic experiences (eg, abuse, neglect, and other negative life events) is associated with physiological dysregulation that increases risk for hypertension and other cardiovascular outcomes.[15]

Using data from the Intergenerational Impact of Genetic and Psychological Factors on Blood Pressure (InterGEN), a longitudinal study of Black mothers and their children, we tested the hypothesis that greater personal exposure to childhood trauma would interact with DNAm to increase BP among Black mothers. Furthermore, because there is limited evidence on the role of vicarious trauma exposure on DNAm,[15] we examined the hypothesis that mothers' report of trauma in

their children would interact with DNAm to increase BP among Black mothers.

Methods

Study sample

Data for the present analysis were from InterGEN study, which aimed to examine genetic (eg, candidate genes, epigenetic effects) and environmental (eg, discrimination, trauma exposure, parenting stress) factors that impact BP in 250 dyads of Black mothers and their children (N = 500). The present sample includes 244 women enrolled in the InterGEN study with complete trauma data.

Briefly, participants were recruited from Early Care and Education Centers that provide preschool education to low-income children as well as community events in southwest and central Connecticut. Recruitment sites were provided with study materials (eg, brochures, flyers) for distribution to potential families. Potential participants were approached by study staff, informed of the study aims, and, if interested, consented for telephone screening to ensure eligibility. Participation was restricted to women who were: (a) ⩾21 years old; (b) identified as African American or Black (via self-report); (c) spoke English; and (d) had a biological child 3 to 5 years old. Participants were excluded if they had a psychiatric or cognitive disorder that limited the accuracy of their self-reported data. Detailed information about InterGEN recruitment has been previously described.[56,57]

All participants provided written informed consent prior to participation in the study. All study procedures were approved by the Institutional Review Board at Yale University. Dyads were followed every 6 months for 18 months to evaluate genetic and environmental factors that may contribute to variations in BP in mothers and children. Mothers were interviewed at baseline and 6-, 12-, and 18-months post-enrollment. Participants were compensated $25 at each assessment. The present study reports on data from the baseline assessment and includes only mothers. Baseline assessments (including clinical data and structured interview) were completed in the community (eg, participants' home, recruitment sties) and took an average of 2 hours to complete.

Clinical data

Clinical data for this analysis were collected at the first of 4 time points in this longitudinal study. After completing informed consent, a trained research assistant measured BP for mother and child using an electronic BP monitor per JNC-7 guidelines.[58] Mothers were instructed to avoid caffeine, exercise, and smoking for at least 30 minutes prior to their visit.[58] (p.7) In accordance with JNC-7 guidelines,[58] they were seated quietly for at least 5 minutes in a chair, with feet on the floor, and their left arm supported at heart level. During the visit, each participant had 3 BP readings recorded on the same arm with each reading at least 5 minutes apart. The 3 readings were used to calculate participants' average systolic and diastolic BP (SBP and DBP).

We measured mothers' weight with a Tanita high-capacity electronic scale (BF-684W/Tanita, Tokyo, Japan). Height was rounded to the nearest 10th of an inch and assessed in barefoot participants using a stadiometer. Weight and height measurements were used to calculate body mass index (BMI; kg/m^2).[59]

Saliva samples were collected from mothers in a standardized manner concurrently with clinical measures at the baseline assessment. Saliva was collected using Oragene (OG)–500 format tubes. Participants were asked to refrain from eating, drinking, smoking, or chewing gum for at least 30 minutes before collecting saliva. They were instructed to spit into the collection tube several times until the contents reached the fill line (2 ml). If participants were unable to produce enough saliva to reach the fill line, they were provided a clear, artificially sweetened lollipop to help stimulate saliva production. All data and specimens from each participant were identified through a unique identifier, which was used for all communications among the study team to identify participants, their samples, and their data. Additional information about data collection methods can be found elsewhere.[56,57]

Measures

Interviews were completed after collection of clinical data. All survey measures were administered in English via Audio Computer-Assisted Self Interviewing software to minimize social desirability bias. A research assistant was present throughout the interview to assist participants if any concerns arose. At the baseline interview, mothers completed background demographic information, the Life Events Checklist [LEC], and the Traumatic Events Screening Inventory—Parent Report Revised [TESI-PRR].

Childhood trauma. The LEC is a widely used and validated self-reported instrument that screens for 17 potentially traumatic events throughout a participant's lifetime.[60] The LEC has been shown to have good internal consistency and adequate test-retest reliability.[60] Mothers were asked to indicate whether they personally experienced each of the 17 potentially traumatic experiences across the lives, such as natural disaster, physical and sexual abuse, and transportation accidents (1 = "Yes"; 0 = No). For every potentially traumatic experience reported, mothers were asked to report the age (in years) at which the event occurred. To assess personal exposure to childhood trauma, we created a dichotomous measure (1 = "Any childhood trauma reported"; 0 = "No childhood trauma reported").

Vicarious trauma. The TESI-PRR is a valid and reliable measure to assess trauma exposure that is completed by the parent or caregiver on behalf of children under the age of 7.[61,62] TESI-PRR test-retest reliability ranges from 0.50-0.79.[61] The TESI-PRR assesses exposure to potentially traumatic experiences

such as injuries, hospitalizations, accidents, and physical and sexual abuse. To assess vicarious trauma, mothers were asked to report whether their child had ever experienced each of the 24 potentially traumatic experiences in the TESI-PRR. Responses to all items were dichotomous (1 = "Yes"; 0 = No). Mothers were assigned a score of "1" for vicarious trauma if they endorsed their child had experienced any trauma and "0" if they endorsed their child had experienced no trauma.

Potential confounders. Participants self-reported their age (in years; continuous) and whether they currently smoked cigarettes (yes/no) at the baseline interview.

Genetic and epigenetic processing

Saliva samples for DNA were transported from the field to the research laboratory where they were refrigerated at 4ºC until DNA extraction and analysis were completed using ReliaPrep™ commercially-available kits. The ReliaPrep™ standard operating procedures guidelines were used to conduct DNA extraction and purification.[63] All tubes and plates containing DNA samples were labeled with barcodes to ensure precise sample tracking. Upon receipt at the laboratory, barcoded samples were into the laboratory's computerized freezer inventory. DNA pipetting was performed with robotic workstations that incorporate barcode scanning to track the transfer of biological material from tube to tube, tube to plate, and plate to plate. These customized barcode scanning programs are integrated with the robotics deck configuration and are networked to the laboratory. Concurrent electronic sample tracking ensured that an individual's DNA in each well of every plate generated could be identified for correct merging to genotype calls. These quality control assurance procedures are monitored frequently and updated as needed for continued improvement of sample management.

The Illumina Infinium Methylation EPIC (850K) BeadChip was used for epigenome wide DNAm measurement.[64] This BeadChip directly quantifies DNAm at 853 307 CpG dinucleotides, giving near complete coverage of known genes. We performed hybridization on a per-sample basis. The Infinium arrays are well annotated for CpG dinucleotides in CpG island and non-CpG island promoters, shore regions, coding regions, repetitive elements, miRNA promoter regions, FANTOM5 enhancers, ENCODE open chromatin and enhancers, and DNase hypersensitivity sites and include 91.1% of the loci from the HumanMethylation450 BeadChip. DNAm is determined at each of the CpG sites on the 850K array by measuring the fluorescent signals from the M (methylated) and U (unmethylated) probes specific for each site included in the array, covering approximately 99% of all RefSeq genes and 96% of CpG islands.[64-66] We confirmed DNAm by methylation-specific polymerase chain reaction (PCR) and by bisulfite sequencing.[67] Quantile-normalization of beta values for autosomal CpG sites was performed. All individual samples (N = 250) passed laboratory based quality control procedures (missing rate <10%). CpG sites were excluded if they had

detection *P*-value greater than .01 (N = 71), had a missing rate greater than 10% (N = 514), overlapped with single nucleotide polymorphisms (N = 14184), or were listed in the recent Illumina quality notice (N = 977). A total of 846 459 autosomal CpG sites were included in the association analyses.

Statistical analysis

We explored the epigenome-wide interaction with both LEC and TESI-PRR scores on SBP and DBP in separate models. Separate linear mixed effects models were fitted at each CpG site with the DNAm beta-value and trauma scores (LEC or TESI-PRR) as predictors and SBP and DBP modeled as dependent variables. An interaction product term between the DNAm beta-value and trauma scores were added to models. We controlled as fixed effect covariates for age, cigarette smoking, and BMI, which are accepted confounders in epigenomic studies. Potential heterogeneity in cell proportions from saliva was corrected using the reference-free EWAS (epigenome-wide association studies) method.[68] A random intercept was added to account for the batch effect. All analyses were conducted in the R statistical computing environment (Version 4.0.3)[69] and selected packages from Bioconductor.

Results

All adult participants with complete data for LEC and TESI-PRR were included in the present study. A total of 244 participants contributed data to this analysis; 227 participants for the LEC analysis and 244 for the TESI-PRR analysis. Six participants were excluded due to missing data for both the LEC and the TESI-PRR. Table 1 presents sample characteristics. LEC and TESI-PRR scores both ranged from 0 to 7. Approximately 45% of women reported at least one form of direct exposure to childhood trauma. Similarly, 49% of women reported at least one form of vicarious trauma. Mean SBP and DBP were 114.0 mmHg (SD = ±13.6) and 72.5 mmHg (SD = ±10.8), respectively.

Tables 2 and 3 present results of linear regression analyses examining the associations of direct and vicarious trauma with SBP and DBP. Neither direct or vicarious trauma were significantly associated with SBP or DBP. Across all models we found that greater age and BMI were significantly associated with higher SBP and DBP.

In our EWAS interaction analysis, we found that there was no significant interaction of direct childhood trauma with DNAm on SBP or DBP (Figure 1). A total of 22 783 and 11 362 CpG sites had marginally significant interaction p-values (*P* < .05) for SBP and DBP, respectively. Similarly, the EWAS analysis examining the interaction of vicarious trauma and DNAm on SBP and DBP found no CpG sites passed the epigenome-wide significance level (Figure 1). A total of 41 769 and 43 399 CpG sites had marginally significant interaction p-values (*P* < .05) for SBP and DBP, respectively.

Table 1. Sample characteristics (N = 244).

	N (%)	MEAN	STANDARD DEVIATION
Age		31.2	5.8
Education		-	-
Less than high school	12 (4.9)		
High school graduate	88 (36.2)		
Some college	81 (33.4)		
Associate's degree	27 (11.1)		
College graduate or higher	35 (14.4)		
Household income		-	-
⩽$15 000	108 (46.0)		
$15 000-$34 999	71 (30.2)		
⩾$35 000	56 (23.8)		
Employed in past 12 month		-	-
Yes	161 (67.4)		
No	78 (32.6)		
Current smoker		-	-
Yes	53 (21.8)		
No	190 (78.2)		
Body mass index (kg/m²)		29.7	8.3
Any direct childhood trauma		-	-
Yes	102 (44.9)		
No	125 (55.1)		
Any vicarious trauma		-	-
Yes	119 (48.8)		
No	125 (51.2)		
Systolic blood pressure	-	114.0	13.6
Diastolic blood pressure		72.5	10.8

Numbers may not sum to 244 due to missing data; Direct childhood trauma was measured with the Life Events Checklist; Vicarious trauma was measured with the Traumatic Events Screening Inventory—Parent Report Revised.

Discussion

To our knowledge this is the first study in any population to simultaneously examine whether direct childhood trauma or vicarious trauma exposure interact with DNAm to influence BP among adults. We found no significant influence of direct childhood trauma on SBP and DBP among Black women. While there are a number of studies examining how childhood trauma can contribute to alterations in physiological systems that persist into adulthood, the literature on how these perturbations influence BP is lacking.[33,43]

Previous EWAS analyses examining the link between childhood trauma and epigenomics in adults of African ancestry have had conflicting findings.[33] For instance, Zannas et al[45] found that cumulative lifetime stress (eg, life-threatening accidents, physical, and sexual abuse) in childhood and adulthood, but not childhood trauma alone, was associated with accelerated epigenetic aging (defined as the difference between DNAm-predicted age minus chronological age) in an urban sample of Black adults (N = 392). In contrast, in a similar sample of low-income adults (N = 169; 89% Black), Mehta et al[44] found that participants with a history of direct childhood trauma had more pronounced DNAm changes relative to participants who reported no childhood trauma (69% vs 34%). These conflicting findings warrant further investigation to clarify potential physiological pathways that contribute to the well-documented health disparities among Black women.

Although we found that the interaction of childhood trauma and DNAm did not influence BP in Black women, investigators have previously identified significant gene-environment interactions for social determinants of health (eg, discrimination, education) on BP among individuals of African ancestry. In analyses of data from the Jackson Heart Study, investigators found that 2 single nucleotide polymorphisms interacted with major life discrimination to influence both SBP and DBP of approximately 3000 Black adults.[70] Moreover, a recent analysis that included over 2500 Black adults found that educational attainment interacted with one single nucleotide polymorphism (rs6687976), such that individuals with less than a high school education had higher DBP.[71] In addition, prior analyses of InterGEN data found that lifetime racial discrimination was associated with DNA hypomethylation at 7 CpG sites of genes implicated in inflammation, CVD, cancer, and asthma.[72] Another analysis of InterGEN data found that Black women who reported greater parenting stress had significant hypomethylation of poly (ADP-ribose) polymerase-1 (*PARP-1*), a gene that plays a role in stress signaling.[73] Given the findings of previous work, future research that investigates the interaction of childhood trauma and DNAm on BP in Black adults is warranted. In particular, researchers should more comprehensively examine exposure to traumatic experiences (eg, timing, frequency, and severity) in childhood and across the lifespan.

Our study has notable strengths. This study focused on Black women, an understudied population within genetics research.[74] Even epigenomic studies on the influence of childhood trauma that have been conducted among Black adults have largely focused on men with limited attention to Black women.[47-49] Although not significant, our findings add to nascent literature on how vicarious trauma and DNAm interact to influence BP in adults. To our knowledge, this is one of the first studies to examine the interactive effects of vicarious trauma

Table 2. Results of linear regression analyses examining the associations of direct childhood trauma with systolic and diastolic blood pressure (N = 227).

	SYSTOLIC BLOOD PRESSURE *B* (95% CI)	*P*	DIASTOLIC BLOOD PRESSURE *B* (95% CI)	*P*
Any direct childhood trauma	−0.58 (−1.73, 0.57)	.32	−0.55 (−1.51, 0.40)	.25
Age (in y)	0.68 (0.41, 0.97)	<.001*	0.52 (0.29, 0.76)	<.001*
Current smoking	3.38 (−0.57, 7.33)	.087	2.09 (−1.19, 5.37)	.21
Body mass index (kg/m²)	0.62 (0.42, 0.81)	<.001*	0.38 (0.23, 0.54)	<.001*
Adjusted R²	23.2%		16.2%	

Direct childhood trauma was measured with the Life Events Checklist.
*P < .05.

Table 3. Results of linear regression analyses examining the associations of vicarious trauma with systolic and diastolic blood pressure (N = 244).

	SYSTOLIC BLOOD PRESSURE *B* (95% CI)	*P*	DIASTOLIC BLOOD PRESSURE *B* (95% CI)	*P*
Any vicarious trauma	−0.20 (−1.29, 0.89)	.72	−0.18 (−1.08, 0.72)	.70
Age (in years)	0.66 (0.39, 0.92)	<.001*	0.51 (0.29, 0.72)	<.001*
Current smoking	2.85 (−0.82, 6.52)	.13	1.45 (−1.58, 4.49)	.35
Body mass index (kg/m²)	0.61 (0.43, 0.80)	<.001*	0.40 (0.25, 0.55)	<.001*
Adjusted R²	23.0%		17.1%	

Vicarious trauma was measured with the Traumatic Events Screening Inventory—Parent Report Revised.
*P < .05.

and DNAm on BP. Given the lack of studies about the impact of trauma exposure on DNAm among Black women,[33] there is a need for future social epigenomics research that investigates the influence of childhood trauma and other adverse experiences (eg, discrimination) on the health on Black women.

Despite these strengths the present study has several limitations. First, our sample was small. This may have limited statistical power to detect significance of interactive effect of childhood trauma and DNAm on BP. In addition, participants in the present study were relatively young and educated (approximately 95% had completed high school). Less than half of our participants reported experiencing direct childhood trauma or vicarious trauma. It is possible that these factors may have influenced our ability to accurately test the link between trauma exposure and BP. Moreover, analyses in the present study were cross-sectional. There is a need for larger longitudinal studies that replicate our analyses to determine the associations of childhood trauma, DNAm, and BP among Black women. Next, our measures of trauma assessed only the presence of different forms of potentially traumatic experiences. Because both measures were dichotomized we were unable to examine the effects of greater severity of direct or vicarious trauma on BP. Future studies should incorporate comprehensive measures of childhood trauma to determine whether severity and/or frequency of

childhood trauma are differentially associated with DNAm and subsequent elevations in BP among Black women. In addition, the InterGEN study did not assess posttraumatic stress symptoms. Prior work has found that women with trauma exposure who have greater posttraumatic stress symptomatology may be at greater risk for incident hypertension.[75] It is likely that posttraumatic stress mediates the influence of trauma exposure on hypertension risk.[15,76] Further, Mehta et al[44] found distinct epigenomic profiles between participants with and without a history of posttraumatic stress among Black adults. Findings from that study indicate that posttraumatic stress may play an important role in epigenetic reprograming among vulnerable adults. This is an important area for future research.

Conclusion

In the present study we examined influence of gene-environment interaction (ie, DNAm × childhood trauma) on BP in a community-based sample of Black women; an understudied population within social epigenomics research. Results of our EWAS interaction analysis indicated there were no significant interactions of direct or vicarious trauma with DNAm on SBP or DBP. This is the first study to simultaneously examine whether direct or vicarious exposure to childhood trauma interacts with DNAm to influence BP in any population. We
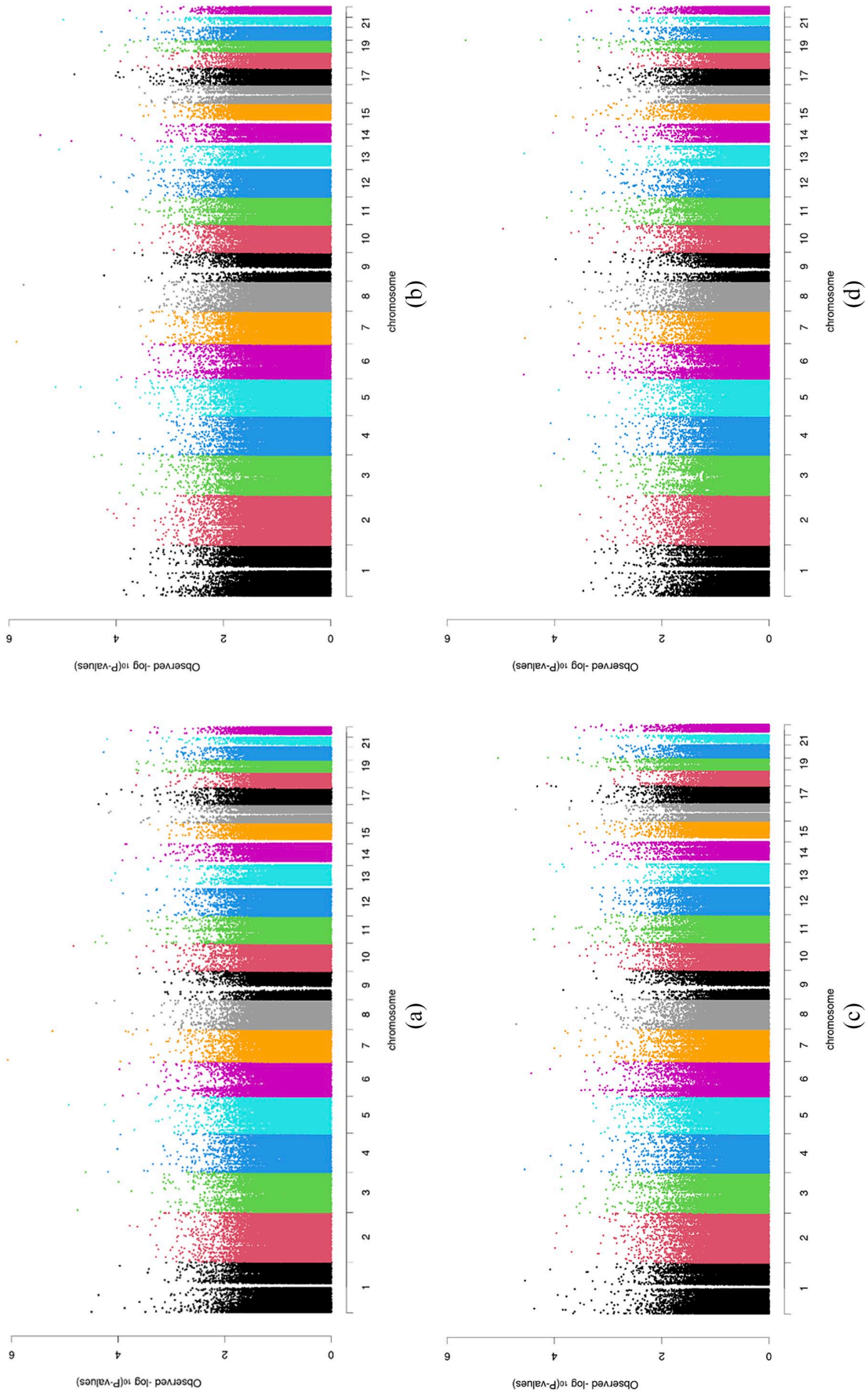
Figure 1. Manhattan plots of epigenome-wide analyses examining the interaction of direct childhood trauma and vicarious trauma with DNA methylation on systolic and diastolic blood pressure.

highlight several recommendations for social epigenomics research. In particular, there is a need for epigenomic studies that comprehensively measure severity and frequency of childhood trauma to determine whether these factors are associated with DNAm and increased BP among Black women.

Author Contributions

Conceptualization, B.A.C., V.B., C.A.C., Y.V.S., and J.Y.T.; investigation, P.A.D.S., and B.I.L.M.M.; data curation, Y.H., Z.W., Y.V.S. and J.Y.T.; writing—original draft preparation, B.A.C., Y.H., V.B., Y.V.S. and J.Y.T.; writing—review and editing, All authors.; project administration, C.A.C. and J.Y.T.; funding acquisition, C.A.C., Y.V.S. and J.Y.T. All authors have read and agreed to the published version of the manuscript.

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