Adverse Childhood Experiences and Blood Pressure Trajectories from Childhood to Young Adulthood: The Georgia Stress and Heart Study

Running title: Su et al.; Childhood Adversity and Blood Pressure Trajectories

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Abstract

Background—The purpose of this study was to assess the long-term effect of adverse childhood experiences (ACEs) on blood pressure (BP) trajectories from childhood to young adulthood and to examine whether this relation is explained by childhood socioeconomic status (SES) and/or risk behaviors that are associated with ACEs.

Methods and Results—Systolic and diastolic blood pressure (SBP and DBP) were measured up to 16 times (13 times on average) over a 23-year period in 213 African Americans (AAs) and 181 European Americans (EAs) aged 5 to 38 years. Retrospective data on traumatic experiences prior to age 18 were collected, including abuse, neglect and household dysfunction. Individual growth curve modeling within a multilevel framework was used to examine the relation between exposure to ACEs and BP development. No main effect of ACEs on average BP levels was found. However, a significant interaction of ACE score with age$^3$ was observed (SBP: $p=0.033$; DBP: $p=0.017$). Subjects who experienced multiple traumatic events during childhood showed a faster rise of BP levels after age of 30 years than those without ACEs. As expected, a graded association of ACEs with childhood SES and negative health behaviors was observed ($p<0.001$). The ACE-SBP relation was not explained by these factors, while the ACE-DBP relation was partially mediated by illicit drug use.

Conclusions—In this novel longitudinal study, we observed that participants who were exposed to multiple ACEs displayed a greater increase of BP levels in young adulthood compared to their counterparts without ACEs.

Key words: adverse childhood experiences, risk behaviors, childhood socioeconomic status, blood pressure, longitudinal cohort study, ethnicity
Introduction

Essential hypertension is a major public health and medical challenge in the United States (US), with one third of US adults having high blood pressure (BP) and only about half of those having it under control. Elevated BP has been associated with increased risk of coronary heart disease (CHD) and stroke, which are leading causes of death and disability in the US.

Previous studies, including ours, have demonstrated that levels of BP track from childhood into adulthood. As a critical developmental phase during which blood pressure levels are programmed, environmental exposures in early life may have a long-term effect on adult BP levels. In fact, growing evidence suggests that traumatic experiences in childhood may contribute to health decline in adult life, including elevated BP levels. For example, studies in Finland have found that children who were separated from parents during World War II showed markedly higher systolic and diastolic blood pressure values in late adult life compared with the non-separated subjects. Socioeconomic adversity in childhood has also been suggested to be an important determinant of increased BP levels in adulthood. However, exposure to low childhood socioeconomic status (SES) is only one marker of early life stress and may not fully represent the psychosocial stress during childhood. Recently, childhood adversity, characterized by abuse, neglect and household dysfunction, is receiving increased attention as an important risk factor for cardiovascular diseases. A national study in nurses has found an association between childhood maltreatment and self-reported hypertension in middle-aged women. However, prospective studies on the association between adverse childhood experiences (ACEs) and BP development are scarce.

Given the deleterious effects of ACEs on public health and the increased risk of adult hypertension among victims exposed to ACEs, the present study investigated the long-term
effect of ACEs on BP trajectories from childhood to young adulthood. In addition, there is evidence indicating that traumatic and stressful events in childhood increase the likelihood of myriad risk behaviors in adolescents and young adults, such as smoking, substance abuse, and physical inactivity, which are also risk factors for high blood pressure. Therefore, we further examined whether the ACE effects on BP development could be explained by childhood SES and negative health behaviors. Moreover, the effect of ACEs on BP development may vary by ethnicity and gender. Adversities in childhood may matter more for minority ethnic groups (e.g. African-Americans) or women’s health. For example, a recent study found that higher parental education levels predicted attenuated BP trajectories in women, but not in men. However, the moderating effect of ethnicity and gender on the relationship between ACEs and BP development has not been explored. Since the present longitudinal cohort consisted of roughly equal number of African-Americans (AAs) and European-Americans (EAs), as well as of males and females, it afforded an opportunity to examine whether the ACE-BP relationship was moderated by ethnicity or gender.

Methods

Subjects

The participants were from the Georgia Stress and Heart (GSH) study, an ongoing longitudinal study evaluating the development of cardiovascular risk factors in youth and young adults. The data encompass a 23-year period (1989 to 2012) in which 16 assessments were conducted. Recruitment and evaluation of participants have been described in detail elsewhere. Briefly, subjects were recruited using family health history questionnaires obtained from a county-wide (Richmond County, Georgia) public school screening of children in grades K through 8 whose
families were interested in health research. All subjects and their parents spoke English as their primary language and all subjects were U.S. born. Participants were classified as AAs if both parents reported being of African heritage and they considered themselves and their child to be AA, black, or Afro-American. Participants were classified as EAs if both parents reported that they were of European ancestry and they considered themselves and their child to be EA, white, or Caucasian, and not of Hispanic, Native American, or Asian descent. On the baseline evaluation, participants who met the following criteria were recruited: (1) aged 5 to 16 years in 1989; (2) AA or EA; (3) normotensive for age and gender based on BP screening; and (4) free of chronic disease based on parental reports of the child’s medical history. The following evaluations were conducted annually from 1989 to 2000 (visit 1-10), every 1.5 year from 2002 to 2006 (visit 11-14) and every 2 years from 2008 to 2012 (visit 15-16). At visit 15, all subjects were 19 years or older and their traumatic experiences prior to age 18 were assessed by using the ACE questionnaire. 11 Out of the 409 subjects recruited at this visit, 394 answered this questionnaire (54% AAs and 53% females). There were no significant differences between those subjects that were excluded (N=15) and those that remained (N=394) in the study with respect to demographic distributions including age, ethnicity and gender. As shown in Supplemental Table 1, all of the 394 subjects had at least 4 visits and 96% of them (N=381) had 8 or more evaluations, which makes this data set very informative for the study of early life stress and blood pressure development over time. In total, the 394 subjects yielded 5017 SBP and DBP measurements, respectively (Supplemental Table 1). The Institutional Review Board at the Medical College of Georgia had given approval for the study. Informed consent was provided by all subjects or by parents if subjects were <18 years. The fact that 78 of the total 394 participants were siblings may have affected the significance of observed effects; when siblings were
excluded from the analyses, however, the results were virtually unchanged, so results for the entire sample are reported here.

**Procedure and Measurements**

On each laboratory visit, the participant was escorted to a quiet, temperature-controlled room where anthropometric and cardiovascular evaluations were conducted using identical protocols by well-trained research staff. Subject’s height and weight were measured with a Healthometer medical scale that was calibrated daily. Body mass index (BMI, kg/m²) was calculated as a measure of general adiposity. The participant was then instrumented for the recording of blood pressure by Dinamap (model 1864 SX). After attachment of an appropriate sized blood pressure cuff to the right arm, the subject was placed in a supine position on a medical table with head propped on a pillow and then given instructions to relax as completely as possible for 15 minutes. Blood pressure measurements were taken from the Dinamap at the end of the 11th, 13th, and 15th minutes. As recommended by the National Health and Nutrition Examination Survey procedures for BP measurement, the average of the last 2 readings was used to represent resting SBP and DBP, respectively.

**Assessment of Adverse Childhood Experiences**

The assessment of participants’ exposure to ACEs covered the first 18 years of their lives. We adapted the questions used in the ACE study. This questionnaire consists of 28 items divided into 3 categories and 10 subscales, including childhood abuse (emotional, physical and sexual), neglect (emotional and physical), and growing up with household dysfunction (substance abuse, mental illness, domestic violence, criminal household member, and parental marital discord).

The definition of ACEs has been described in the **Supplemental Table 2**. As in previous ACE studies, the ACE score (the number of 10 ACE subscales reported) was used to assess the
cumulative effect of multiple ACEs, by classifying respondents into four groups: no exposure (0 ACEs, N=122, coded as 0), low (1-2 ACEs, N=149, coded as 1), moderate (3 ACEs, N=49, coded as 2), and severe (≥4 ACEs, N=74, coded as 3) exposure (Figure 1).

**Childhood Socioeconomic Status**

Childhood socioeconomic status (SES) was represented by the Hollingshead Four Factor Social Status Index on the basis of parental education levels and occupations. The value measured at the midpoint of the study was taken as representative for the whole study period. The Hollingshead scores ranged from 14 to 66, with higher scores representing greater childhood SES. To illustrate the BP trajectories according to childhood SES, the Hollingshead scores were divided into tertiles, indicating high (coded as 0), medium (coded as 1) and low (coded as 2) levels of childhood SES. We further calculated a composite score of exposure to ACEs (0-3) and childhood SES (0-2) by summarizing these two scores, which ranges from 0 (i.e. no ACE exposure and high childhood SES) to 5 (i.e. severe exposure to ACEs and low childhood SES).

**Negative Health Behaviors**

Physical activity (PA) was assessed by the self-reported number of days per week, in or outside of school, during which PA that was sufficient to “work up a sweat” was performed. The average of PA days across all the visits was used to represent the participant’s regular PA. This measure has been validated previously with more comprehensive self-report measures of sedentary behavior. To illustrate the PA levels on BP trajectories, the PA levels were defined as high (sufficient PA for 5-7 days/week, coded as 0), medium (sufficient PA for 2-4 days/week, coded as 1) and low (sufficient PA for 0-1 days/week, coded as 2), respectively. In the present study, about 25% of subjects had low PA and 11% had high PA. At each visit, participant’s smoking status was assessed by the self-reported number of days smoked during the
past 30 days and the number of cigarettes smoked per day. The subjects who smoked ≥1 cigarettes in the past 30 days at any visit were considered as smokers. Thirty nine percent (N=155) of participants were current or previous smokers. In addition, the participants were also asked whether they used illicit drugs in the past 30 days, including marijuana, cocaine, sniffed glue, or methamphetamines. Out of 394 subjects, 122 (31%) reported to use at least one of these illicit drugs at one or more visits. Past research suggested that these measures of tobacco and illicit drug use in youth were both reliable and valid. 26

**Statistical Analyses**

All descriptive analyses were done using STATA software. The effects of gender and ethnicity on the distributions of general characteristics at the participants’ first evaluation were examined by using linear regression for quantitative traits (e.g. BMI, SBP, DBP, Hollingshead index and physical activity) or logistic regression for binary traits (e.g. smoking and illicit drug use) with the adjustment for age. Gender and ethnicity differences in prevalence of ACE scores were examined by using ordinal logistic regression adjusted for age. The relationship of ACE exposure with childhood SES, as well as with PA levels, smoking and use of illicit drugs, were examined by using linear regression or logistic regression with the adjustment for age, race and gender.

*Growth curve modeling*

The effect of ACEs on the development of SBP and DBP from childhood to adulthood was examined using individual growth curve modeling within a multilevel framework, which is a data analysis technique especially designed for longitudinal data. 19 Such data can be considered to be clustered or hierarchical data since repeated observations (first level) are nested within subjects (second level). Individual growth curve modeling accounts for the dependency of the
data owing to this clustering, and fits a curve for each individual. These individual growth curves (e.g. SBP and DBP development with age) are characterized by their intercept (or level) and slope (rate of change). Addition of independent variables to the model, such as ACE exposures, is aimed at explaining between-subject variation (in level and slope) of the BP growth curves.  

Analytical strategy

Repeated BP measurement was regarded as a 2-level hierarchy, with subjects at level 2 (between-subject level) and repeated measurements (or visits) at level 1 (within-subject level). We first specified the unconditional growth model, in which fixed and random linear, quadratic, and cubic trends were fitted by the addition of, respectively, age, age² (age×age), and age³ (age×age×age) to the intercept-only model. Age was expressed as a deviation from its mean of 19.5 years. Ethnicity and gender were then added to the unconditional growth model to test the effects on BP development, the latter modeled as interaction with age, age², and age³. The interaction between ethnicity and gender was also tested. Next, BMI was added to the model to estimate the effect on BP development. In addition to the main effect, we also tested whether interactions of BMI with age, ethnicity and gender affected the growth curve. All variables that had significant effects on BP development in the previous models were entered simultaneously as a full model. In the final step, ACE score was added to the model as a categorical variable, followed by their respective interactions with age, age² and age³, as well as their respective interactions with ethnicity and gender, to test whether BP grows differently by individual exposure to ACEs.

A likelihood ratio test was used to determine the significance of the fixed and random effects that were added to the model in each of the analysis steps. This test yields the deviance of the model which is defined as -2×loglikelihood. The deviance difference (between 2 models) is
asymptotically $\chi^2$ distributed, with the number of degrees of freedom equal to the difference in number of estimated parameters between the 2 models. To judge the significance of parameters in the full model, each parameter was removed from the model, and a likelihood ratio test with 1 degree of freedom was used to examine whether its effect was significant in this full model.

Multilevel modeling was performed using the program MLwiN. 27

Categorized childhood SES (high: 0; medium: 1; low: 2), PA levels (high: 0; medium: 1; low: 2), smoking (no: 0; yes: 1) and use of illicit drugs (no: 0; yes: 1), as well as their interactions with age, age$^2$ and age$^3$, were further added to the BP growth-curve models to test whether they contributed to BP development and whether the ACE-BP relation was independent of these factors. The interactions of risk behaviors and ACEs were also examined. Furthermore, we examined the composite effect of exposure to ACEs and childhood SES on BP trajectories by using the composite scores as calculated above.

**Results**

Descriptive characteristics by ethnicity and gender at participants’ first evaluation are shown in Table 1. Compared to EA youth, AA youth had significantly higher BMI, SBP, DBP and lower childhood SES (p<0.001). EA youth performed more exercise than AA youth (p=0.001). However, more EA youth were smoking (p<0.001) and using illicit drugs (p=0.055). Females had higher BMI and DBP, but lower SBP than males. Compared to males, females performed less exercise, lower rate of smoking and use of illicit drugs (p<0.001). Of note, participants were still relatively young at their last evaluations, with mean age of 30 years old (age range: 20-38 years old).

**Prevalence of ACEs**

The prevalence of each individual ACE subscale is shown in Figure 1, with the lowest
prevalence of physical neglect (9.4%) and the highest prevalence of parental marital discord (38.2%). Overall, 69% of respondents reported at least one exposure to ACEs, with mild (1-2 ACEs), moderate (3 ACEs), and severe (≥4 ACEs) exposure to ACEs representing 37.9%, 12.5% and 18.8%, respectively (Figure 1). As shown in Table 1, the prevalence of ACE exposure was similar between males (69.4%) and females (68.8%), but slightly higher in AAs (72.8%) than in EAs (64.6%). AA males had the highest prevalence of severe exposure to ACEs (ACE score ≥4, 28.1%) compared to the other three groups.

ACEs, Childhood SES and Negative Health Behaviors

A graded association of the ACE scores with childhood SES and negative health behaviors was observed, except for physical inactivity (Table 2). Subjects who were exposed to more ACEs showed significantly lower childhood SES. The prevalence of smoking and using illicit drugs was increased 2- and 2.5-fold among persons with ≥4 ACEs compared to those with 0 ACEs. Adjustment for age (at the 15th visit when ACEs were assessed), ethnicity and gender did not change the results.

ACEs and Systolic/Diastolic Blood Pressure Growth Curves

Figure 2 and 3 depict the results for the analyses of ACE effects on the development of SBP and DBP based on the most parsimonious full model shown in the footnote. No main effect of ACEs on BP average levels was found. However, a significant interaction of ACE score with age was observed (SBP: β=0.0004617, se=0.0002155, p=0.033; DBP: β=0.0003864, se=0.0001609, p=0.017). Young adults who experienced multiple traumatic events during childhood showed a faster increase of BP levels than those with no ACEs. Notably, these differences were observable after the age of 30 years. Based on the prediction model, at the age of 38 years, subjects with ≥4 ACEs had average SBP and DBP levels 9.3 mmHg and 7.6 mmHg higher, respectively, than
those with 0 ACEs, after controlling for ethnicity, gender and BMI. No significant interactions of ACE score with ethnicity and gender were found (data not shown), indicating that the exposure to ACEs had similar effects on BP development of EAs and AAs, as well as of males and females.

Because of the inexact knowledge of when the traumatic events occurred before age 18 years, there may have been a mismatch between ACE exposure and BP measurement during childhood. Therefore, we repeated all analyses among subjects at 18 years or older, which yielded 2830 SBP and DBP measurements. As shown in Figure 4 and 5, similar ACE effects were found on SBP and DBP growth curves (i.e. significant interaction with age\textsuperscript{2} in this case), indicating that subjects who were exposed to ACEs had a higher increase of BP in young adulthood compared to those with no ACEs.

**Effects of Risk Behaviors**

In the SBP growth model, no significant main effects or interactions with age were found for behavioral risk factors including physical inactivity, smoking and use of illicit drugs. After controlling for these factors, the association between ACEs and SBP trajectories was virtually unchanged. For DBP, a significant interaction of illicit drug use with age was observed ($\beta$=0.1341, se=0.0443, p=0.002), suggesting a greater increase of DBP among subjects who used illicit drugs (Supplemental Figure 1). After adjusting for this factor and its interaction with age, the association between ACEs and DBP growth was attenuated, but still significant (ACEs $\times$ age\textsuperscript{3}: $\beta$=0.0003179, se=0.0001618, p=0.04). Furthermore, there were no significant interaction effects between risk behaviors and ACEs on BP development.

**ACEs, Childhood SES and BP Trajectories**

To distinguish the effects of ACE exposure and childhood socioeconomic disadvantage, we
further examined the relationship between childhood SES and BP trajectories over time. Similar to the effect of ACEs on SBP, a significant interaction of childhood SES with age$^3$ was observed for SBP ($\beta=0.00111$, se=0.000481, $p=0.022$) (Supplemental Figure 2), but not for DBP. However, after adding ACE score and childhood SES simultaneously into the model, both effects were attenuated and not significant (ACEs × age$^3$: $\beta=0.0003304$, se=0.0002272, $p=0.14$; childhood SES × age$^3$: $\beta=0.0005181$, se=0.0003015, $p=0.08$), which might be due to the collinearity between these two factors (Spearman $\rho=0.3$, $p<0.001$). We further examined the composite score of exposure to ACEs and childhood SES, and found a significant interaction of this score with age$^3$ on SBP ($\beta=0.0004057$, se=0.00015, $p=0.006$) and on DBP ($\beta=0.0002299$, se=0.0001126, $p=0.03$), respectively. Given the fact that 35% of the participants with ≥4 ACEs were coming from medium or high SES families, and one third had no history of ACEs but had low SES, our results suggested that these two factors were linked but were not redundant.

Discussion

Taking advantage of a longitudinal cohort composed of EA and AA boys and girls who were followed-up for 23 years (1989-2012) with up to 16 assessments (13 on average) of blood pressure, for the first time, we found a significant association between the number of ACEs and BP trajectories from childhood to young adulthood. Participants who experienced multiple traumatic events prior to age 18 showed greater increases of BP levels in young adulthood compared with those who were not exposed to ACEs. The enduring consequences of ACEs were not fully explained by established concurrent risk factors such as childhood SES, smoking and use of illicit drugs. In addition, no significant interactions of ACEs with ethnicity or gender on BP development were observed, suggesting a similar effect of ACEs for BP across different population groups.
Major Features

One unique and important feature of the present study is that it involved blood pressure measured every one or two years over a 23-year period from childhood to young adulthood. The analytical strategy we employed, i.e. the multilevel growth-curve modeling, enabled us to investigate the influence of early life stress in the development of BP over time. Previous studies have suggested that psychosocial factors and stress in early life contribute to hypertension in adults, while the history of hypertension was self-reported. The present study confirmed and extended previous findings. This study demonstrated that young adults who were exposed to ACEs had a more rapid rise of BP levels in the third decade of life, suggesting ACE exposure results in a higher risk for developing hypertension, most likely at an earlier age, than their counterparts without a history of ACEs. Moreover, consistent with previous findings, children exposed to a greater number of adverse experiences have a greater increase of both SBP and DBP in young adult life, suggesting a cumulative effect of childhood adversities on BP development over time.

The second feature of the present study is that we evaluated participants’ early family environments by including the assessments of both childhood SES and traumatic experiences with respect to abuse, neglect and household dysfunction. Our results indicate that groups of children exposed to adverse events and low SES do not necessarily overlap. For example, 50% of our participants with a history of childhood abuse and 40% of children being neglected were coming from medium or high SES families, which agrees with previous findings. Consequently, exposure to ACEs may exert effects on BP trajectories that is independent of childhood SES. ACE exposures contributed to the development of both SBP and DBP while childhood SES was only associated with SBP growth but not DBP. Relieving childhood poverty
alone may be insufficient to eliminate the BP-related health problems associated with adverse childhood experiences.

The third unique feature of the present study cohort is that it incorporated roughly equal numbers of EAs and AAs, as well as of males and females. In line with previous research with this cohort,\textsuperscript{5,19} we found significant differences in average BP levels emerged by ethnicity and gender from early adolescence onward, with AAs having higher SBP and DBP than EAs, and males having higher SBP but lower DBP than females. Although AAs had a slightly higher prevalence of exposure to ACEs than EAs, there was no significant difference of ACEs on BP trajectories between the two ethnic groups. A recent study suggested that gender might modify the association between childhood SES and BP trajectories. Increasing parental education was associated with flatter SBP and DBP growth among women but not men.\textsuperscript{18} In the present study, however, no significant interaction was found between gender and ACEs on BP development, suggesting that exposure to ACEs may have similar effects on BP growth from childhood to young adulthood in males and females.

Mechanisms Linking ACEs to Elevated Blood Pressure

Unhealthy behaviors

Multiple ACEs indicate a harsh and stressful environment and early exposure to ACEs can lead to adoption of risky lifestyle behaviors such as smoking and substance abuse.\textsuperscript{13} Some studies,\textsuperscript{11,12} but not all,\textsuperscript{10} have suggested that the relation of ACEs to poor health outcomes were, at least partially, mediated by risk behaviors. In the present study, although a graded association of ACE score with unhealthy behaviors was observed, the ACE-BP relation was mostly independent of these factors. Only, use of illicit drugs had a significant influence on DBP trajectories over time and partially mediated the association between ACEs and DBP growth. Of note, participants in
the present study were still relatively young at the end of this study; therefore the influences of
risk behaviors on BP may not be so significant. As these subjects continue to age, risk behaviors
may play an increasingly important role in middle or late adulthood.

*Physiological pathways*

Given the fact that multiple systems, e.g. nervous, endocrine and immune systems, are not fully
developed at birth and show profound changes during childhood, adversities in early life may
shape the experience-dependent maturation of stress-related pathways underlying these systems,
leading to long-lasting altered stress responsivity in adulthood. 29 Indeed, traumatic experiences
in childhood have been associated with hyperactivity of the hypothalamic-pituitary-adrenal axis
and sympathetic nervous system, as well as elevated inflammation in adults. 30-32 Alterations in
these systems may mediate the effect of early life stress on the dysregulation of blood pressure.

In addition, BMI is a major determinant of BP development. Previous reports showed that
children with a history of physical abuse were more likely to have higher BMI as adults than
those with no exposure to abuse. 33 In the present study, adjustment for BMI did not change the
association between ACEs and BP trajectories, suggesting that adverse experiences prior to age
18 may affect BP development in young adults through a mechanism independent of BMI. Most
recently, our studies in rats and humans suggested that exposure to early life stress may induce
elevated plasma endothelin-1 (ET-1) levels, indicating that the ET-1 pathway may underlie the
link between early trauma and later development of blood pressure. 34,35

*Limitations*

Our study has several limitations. First, similar to previous large cohort studies, the individual’s
experiences of childhood adversity were collected based on retrospective self-report. Because of
the sensitive nature of questions about ACEs and affective problems, the responses probably
represent an under-reporting of their actual occurrence. However, given the established relationship between ACE and the risk for cardiovascular disease development, the under-reporting of the adversities, if it exists, should have weakened the associations we found here, not exaggerated them. Second, we assessed participants’ adverse experiences prior to age 18, but without exact knowledge of the timeframe these adversities occurred. There may be a mismatch between ACE exposure and BP measurement during childhood. However, by limiting to subjects ≥18 years old, repeated analyses revealed similar relations of ACE scores with BP trajectories over time, suggesting that traumatic experiences in early life may contribute to the increase of BP in young adulthood. Third, subjects with hypertension and other chronic diseases were excluded from the baseline recruitment. It may constrain the variance of the ACE exposure and induce some selection bias as children who experience the greatest degree of adversity early in life may also be unhealthier. Given the fact that this sub-population may have the highest risk to develop cardiovascular disease in adulthood, exclusion of these subjects would be predicted to weaken, not exaggerate, the association between ACE exposure and BP development. Fourth, the effects of emotional factors such as depression and anxiety were not evaluated in the present model. Previous studies have suggested that early life stress may exert effects on adult health outcomes, in part by compromising emotional functioning across the life span. The role of emotional factors in the relation of ACE and BP trajectories is warranted further investigation in the future as this longitudinal cohort continues. Finally, the sample size of the present study was relatively small. Although we assessed BP in up to 16 visits (13 visits on average) and had sufficient power to detect the effect of ACEs on BP growth, we may not have had enough power to detect the significant interactions of ACEs with ethnicity and gender on BP development. In addition, we found that the effects of ACEs and childhood SES on BP trajectories were not
independent of each other. Although it might be due to the high correlation between these two factors, we may also have insufficient power to distinguish their effects. Larger sample size and longer follow-up are warranted in future research.

Conclusions

The present study provides a unique opportunity to assess the relationship between childhood adversities and the longitudinal BP trajectories from childhood to young adulthood. The data are consistent with previous research on the role of early life stress in the pathogenesis of hypertension and further demonstrate that young adults who experienced multiple traumatic events in childhood already display elevated BP levels compared to their counterparts without a history of ACEs. The enduring consequences of ACEs were similar in EAs and AAs, as well as in males and females, and were not fully explained by childhood SES and unhealthy behaviors. Of note, participants in the present cohort were still relatively young at the end of this study. Experiencing childhood adversity may contribute to elevations in hypertensive risk earlier in the life course than previously thought or expected. Identification and early intervention in young adults with experiences of childhood adversity may provide an important avenue for lessening the burden of cardiovascular disease in later adult life.

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Conflict of Interest Disclosures: None.

References:


12. Riley EH, Wright RJ, Jun HJ, Hibert EN, Rich-Edwards JW. Hypertension in adult survivors
of child abuse: observations from the Nurses' Health Study II. *J Epidemiol Community Health.* 2010;64:413-418.


Table 1. Descriptive characteristics of 394 participants by ethnicity and gender at the first evaluation.

<table>
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<th></th>
<th>European-American</th>
<th>African-American</th>
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<tr>
<td>N</td>
<td>97</td>
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<td>31 (36.9)</td>
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<td>37 (38.14)</td>
<td>34 (40.48)</td>
<td>30 (33.71)</td>
</tr>
<tr>
<td></td>
<td>9 (9.28)</td>
<td>9 (10.71)</td>
<td>12 (13.48)</td>
</tr>
<tr>
<td></td>
<td>16 (16.49)</td>
<td>12 (14.29)</td>
<td>25 (28.09)</td>
</tr>
</tbody>
</table>

* Mean value (SD) at the first evaluation; † Mean value (SD) at the midpoint of the study; ‡ Adjusted for age for all variables except for age

DOI: 10.1161/CIRCULATIONAHA.114.013104
Table 2. Relationships of exposure to ACEs with childhood SES and negative health behaviors.

<table>
<thead>
<tr>
<th>Adverse Childhood Experiences</th>
<th>P value‡</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0</td>
</tr>
<tr>
<td>N</td>
<td>122</td>
</tr>
<tr>
<td>Parental Hollingshead Index†</td>
<td>45.0 (12.62)</td>
</tr>
<tr>
<td>Physical activity, days/week†</td>
<td>2.94 (1.46)</td>
</tr>
<tr>
<td>Smoking, N (%)</td>
<td>38 (31.2)</td>
</tr>
<tr>
<td>Using of illicit drugs, N (%)</td>
<td>25 (20.5)</td>
</tr>
</tbody>
</table>

† Mean (SD) was presented.
‡ Adjusted for age (at the 15th visit when ACEs were collected), ethnicity and gender

Figure Legends:

Figure 1. Prevalence of adverse childhood experiences (ACEs).

Figure 2. The predicted systolic blood pressure with age by the number of adverse childhood experiences. Based on the full model: \( SBP = 102.6 \, \text{cons} + 0.194 \, \text{age} - 0.0374 \, (\text{age}^2) + 0.00163 \, (\text{age}^3) + 4.18 \, \text{ethnicity} - 1.782 \, \text{gender} + 0.293 \, \text{age} \times \text{ethnicity} - 0.258 \, \text{age} \times \text{gender} + 0.0331 \, (\text{age}^2 \times \text{gender}) + 0.458 \, \text{BMI} - 0.254 \, \text{BMI} \times \text{gender} + 0.172 \, \text{ACE} + 0.000462 \, (\text{age}^3 \times \text{ACE}). \) Note: age was centered in the model by minus the mean age 19.49. Growth curves represent no exposure to ACEs, 1-2 ACEs, 3 ACEs and ≥4 ACEs (from bottom to top at the age of 38 years old).

Figure 3. The predicted diastolic blood pressure with age by the number of adverse childhood experiences. Based on the full model: \( DBP = 60.16 \, \text{cons} + 0.529 \, \text{age} + 0.0302 \, (\text{age}^2) - 0.00175 \, (\text{age}^3) + 3.56 \, \text{ethnicity} + 6.033 \, \text{gender} + 0.155 \, \text{age} \times \text{ethnicity} - 0.0215 \, (\text{age}^2 \times \text{gender}) - 0.0794 \, \text{BMI} + 0.00649 \, \text{BMI} \times \text{age} - 0.151 \, \text{BMI} \times \text{gender} + 0.102 \, \text{ACE} + 0.000462 \, (\text{age}^3 \times \text{ACE}). \)
0.000386 \text{(age}^3 \times \text{ACE}). \text{Note: age was centered in the model by minus the mean age} 19.49. 

Growth curves represent no exposure to ACEs, 1-2 ACEs, 3 ACEs and \geq 4 ACEs (from bottom to top at the age of 38 years old).

**Figure 4.** The predicted systolic blood pressure with age after 18 years old by the number of adverse childhood experiences. Based on the full model: 
\[
\text{SBP} = 102.3 \text{ (cons)} + 0.0131 \text{ (age)} - 0.00532 \text{ (age}^2) + 5.341 \text{ (ethnicity)} - 1.856 \text{ (gender)} + 0.362 \text{ (age \times ethnicity)} + 0.491 \text{ (BMI)} - 0.257 \text{ (BMI \times gender)} - 0.327 \text{ (ACE)} + 0.0171 \text{ (age}^2 \times \text{ACE}).
\] 
\text{Note: age was centered in the model by minus the mean age} 23.67. Growth curves represent no exposure to ACEs, 1-2 ACEs, 3 ACEs and \geq 4 ACEs (from bottom to top at the age of 38 years old).

**Figure 5.** The predicted diastolic blood pressure with age after 18 years old by the number of adverse childhood experiences. Based on the full model: 
\[
\text{DBP} = 62.75 \text{ (cons)} + 0.847 \text{ (age)} - 0.0125 \text{ (age}^2) + 4.285 \text{ (ethnicity)} + 5.564 \text{ (gender)} + 0.148 \text{ (age \times ethnicity)} - 0.234 \text{ (age \times gender)} - 0.0433 \text{ (BMI)} - 0.162 \text{ (BMI \times gender)} + 0.173 \text{ (ACE)} + 0.0101 \text{ (age}^2 \times \text{ACE}).
\] 
\text{Note: age was centered in the model by minus the mean age} 23.67. Growth curves represent no exposure to ACEs, 1-2 ACEs, 3 ACEs and \geq 4 ACEs (from bottom to top at the age of 38 years old).
Figure 1
Figure 2
Figure 3

ACE scores

DBP, mmHg

Age, years

≤10 12 14 16 18 20 22 24 26 28 30 32 34 36 38
Figure 4

ACE scores

- 0
- 1-2
- 3
- 4+

SBP, mmHg

Age, years

100 102 104 106 108 110 112

18 20 22 24 26 28 30 32 34 36 38
Figure 5
Adverse Childhood Experiences and Blood Pressure Trajectories from Childhood to Young Adulthood: The Georgia Stress and Heart Study
Shaoyong Su, Xiaoling Wang, Jennifer S. Pollock, Frank A. Treiber, Xiaojing Xu, Harold Snieder, W. Vaughn McCall, Michael Stefanek and Gregory A. Harshfield

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Supplemental Table 1. The number and percentage of all the 394 subjects who had blood pressure measured multiple times over a 23-year period

<table>
<thead>
<tr>
<th>Number of BP assessments</th>
<th>Number of subjects</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>394</td>
<td>100</td>
</tr>
<tr>
<td>2</td>
<td>394</td>
<td>100</td>
</tr>
<tr>
<td>3</td>
<td>394</td>
<td>100</td>
</tr>
<tr>
<td>4</td>
<td>394</td>
<td>100</td>
</tr>
<tr>
<td>5</td>
<td>393</td>
<td>99.75</td>
</tr>
<tr>
<td>6</td>
<td>392</td>
<td>99.49</td>
</tr>
<tr>
<td>7</td>
<td>390</td>
<td>98.98</td>
</tr>
<tr>
<td>8</td>
<td>381</td>
<td>96.70</td>
</tr>
<tr>
<td>9</td>
<td>362</td>
<td>91.88</td>
</tr>
<tr>
<td>10</td>
<td>326</td>
<td>82.74</td>
</tr>
<tr>
<td>11</td>
<td>307</td>
<td>77.92</td>
</tr>
<tr>
<td>12</td>
<td>272</td>
<td>69.04</td>
</tr>
<tr>
<td>13</td>
<td>211</td>
<td>53.55</td>
</tr>
<tr>
<td>14</td>
<td>189</td>
<td>47.97</td>
</tr>
<tr>
<td>15</td>
<td>143</td>
<td>36.29</td>
</tr>
<tr>
<td>16</td>
<td>75</td>
<td>19.04</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>5,017</strong></td>
<td></td>
</tr>
</tbody>
</table>
# Supplemental Table 2. Definition and prevalence of each category of ACE and ACE Scores

<table>
<thead>
<tr>
<th>Category</th>
<th>Exposed to ACEs</th>
<th>Prevalence (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Abuse</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Emotional</td>
<td>Did a parent or other adult in the household, never, sometimes, often or very often Respond “often” or “very often” to either question</td>
<td>12.76</td>
</tr>
<tr>
<td>Physical</td>
<td>Did a parent or other adult in the household, never, sometimes, often or very often Respond “often” or “very often” to the first question or “sometimes, often, or very often” to the second</td>
<td>17.60</td>
</tr>
<tr>
<td>Sexual</td>
<td>Did an adult or person at least 5 years older ever Respond affirmatively to any of these questions</td>
<td>16.33</td>
</tr>
<tr>
<td><strong>Neglect</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Emotional</td>
<td>Following statement is never, sometimes, often, very often true. Questions were reverse-scored and summed on a Likert scale. Persons with a score of 15 or higher (moderate or extreme) were considered to have experienced emotional neglect.</td>
<td>11.42</td>
</tr>
<tr>
<td>Physical</td>
<td>Following statement is never, sometimes, often, very often true. Questions were scored and summed on a Likert scale, with questions 2 and 5 reverse-scored. Persons with a score of 10 or higher (moderate or extreme) were considered to have experienced physical neglect.</td>
<td>9.39</td>
</tr>
<tr>
<td><strong>Household dysfunction</strong></td>
<td>Have you lived with anyone who Respond affirmatively to either</td>
<td>26.90</td>
</tr>
<tr>
<td>Question</td>
<td>Subscale</td>
<td></td>
</tr>
<tr>
<td>-------------------------------------------------------------------------</td>
<td>----------</td>
<td></td>
</tr>
<tr>
<td>(1) Was a problem drinker or alcoholic?</td>
<td>Mental illness</td>
<td></td>
</tr>
<tr>
<td>(2) Used street drugs?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mental illness</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Have you lived with anyone who</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(1) Was depressed or mentally ill?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(2) Attempted suicide?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Domestic violence</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Was your mother (or stepmother), never, sometimes, often or very often</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(1) pushed, grabbed, slapped, or had something thrown at her?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(2) kicked, bitten, hit with a fist, or hit with something hard?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(3) repeatedly hit over at least a few minutes?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(4) threatened with or hurt by a knife or gun?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Criminal household member</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Did a household member go to prison?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Parental marital discord</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Were your parents ever separated or divorced?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ACE Score (the number of subscales of ACEs reported)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>0 (n=122)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1-2 (n=149)</td>
<td>30.96</td>
<td></td>
</tr>
<tr>
<td>3 (n=49)</td>
<td>37.82</td>
<td></td>
</tr>
<tr>
<td>4+ (n=74)</td>
<td>12.44</td>
<td></td>
</tr>
<tr>
<td></td>
<td>18.78</td>
<td></td>
</tr>
</tbody>
</table>
Supplemental Figure 1. The predicted diastolic blood pressure with age by use of illicit drugs.
Supplemental Figure 2. The predicted systolic blood pressure with age by the childhood SES levels. Growth curves (from bottom to top at the age of 38 years old) represent high, medium and low levels of childhood SES.