Childhood Trauma is Associated with Perceived Stress and Hair Cortisol Level Characterized by BDNF Val66Met Genotype and Sex

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A Master's Thesis Submitted
to the Department of Medicine
and the Graduate School of Yonsei University
in partial fulfillment of the
requirements for the degree of
Master of Medical Science

Zhenxu Li
December 2024

This certifies that the Master's Thesis of Zhenxu Li is approved.

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The Graduate School
Yonsei University
December 2024

ACKNOWLEDGEMENTS

I want to express my deepest gratitude to everyone who has contributed to completing this work. First and foremost, I wish to thank my supervisor, Professor Suk Kyoon An, for his invaluable guidance and support throughout my research. My gratitude to him is beyond words, and I attempt to express it through a poem: “How can I gaze up at the lofty mountain? I can only bow in respect, hoping to catch a hint of its fragrance.” Professor An embodies this idea, setting an inspiring example from whom I am humbled to learn. He has provided me with the motivation and courage that means so much to a beginner; only with his support have I found the strength to pursue my path in psychiatry. I am also immensely grateful to my lab members, Se Jun Koo, Hye Yoon Park, and Ji Eun Min, who contributed to data collection and provided constructive feedback. I would also like to thank the review committee members sincerely, Professor Eun Lee and Professor Jung Tak Park, who took time from their busy schedules to review my thesis and provide valuable feedback. Special thanks to my friends in Korea and abroad. I am grateful to have them in my life. Finally, I would like to thank my parents for their unwavering support and love.

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ABSTRACT

Childhood Trauma is Associated with Perceived Stress and Hair Cortisol Level Characterized by BDNF Val66Met Genotype and Sex

Childhood trauma increases the risk of mental disorders by affecting both psychological and physiological stress responses in adulthood, including perceived stress and long-term hypothalamic-pituitary-adrenal (HPA) axis activity. The mechanisms underlying these effects may involve gene-environment (G × E) interactions, with the brain-derived neurotrophic factor (BDNF) gene Val66Met polymorphism and sex playing important roles. The author aimed to investigate how childhood trauma influences stress responses, considering the BDNF Val66Met polymorphism and sex differences.

Secondary data from 190 healthy young adults (96 women) were analyzed. Childhood trauma and perceived stress were assessed using the Childhood Trauma Questionnaire (CTQ) and the Perceived Stress Scale (PSS), respectively, and hair cortisol concentration (HCC) was assessed as a measure of long-term cortisol levels. Participants were genotyped for the BDNF Val66Met polymorphism and stratified as Val/Val or Met carriers. Hierarchical linear regression models were used to examine the interactions between CTQ score, BDNF Val66Met genotype, and sex to assess their effects on PSS score and HCC. Additional analyses included separate linear regression models of the CTQ score for HCC in Val/Val and Met carriers according to sex.

Higher CTQ scores were positively associated with PSS scores in the entire sample. No significant main effects of CTQ score, BDNF Val66Met genotype, or sex on HCC were observed. However, a significant three-way interaction between CTQ score, BDNF Val66Met, and sex was observed in patients with HCC, with a positive association between HCC and childhood trauma observed exclusively in Val/Val carriers.

This study demonstrated that childhood trauma elevates perceived stress across all participants and increases HCC levels specifically in women Val/Val carriers, highlighting the role of childhood trauma, BDNF Val66Met, and sex in shaping stress responses. Taken together, these findings underscore the importance of considering genetic and sex factors when examining the long-term effects of childhood trauma on the HPA axis. Further research is required to elucidate the underlying mechanisms in populations with diverse age stages and clinical conditions.

Keywords: BDNF, Val66Met, Childhood trauma, Perceived stress, Hair cortisol concentration

1 INTRODUCTION

Childhood trauma, including physical, emotional, and sexual abuse, as well as physical and emotional neglect [1], is strongly associated with increased vulnerability to mental disorders such as depression [2], schizophrenia [3], and post-traumatic stress disorder (PTSD) [4]. The underlying pathways are unclear and may involve altered psychological and physiological stress response, with childhood trauma being considered as an environmental stressor [5,6]. Psychological responses to stress play a critical role in the development of mental illness [7,8] and these responses can be influenced by childhood trauma. According to the stress sensitization framework [9], childhood trauma has long-term impacts on psychological sensitivity to stress. Cumulative advantage/disadvantage theory [10] suggests that individuals with childhood trauma may encounter a series of disadvantages later in life, indicating that stress can accumulate over time. Combined with numerous studies supporting the connection between childhood trauma and increased perceived stress in adulthood [11,12], individuals with childhood trauma tend to perceive stress as overwhelming and adopt negative coping strategies [13], leading to a cycle of increased stress and heightened stress perception over time. Therefore, childhood trauma profoundly affects psychological stress responses, including perceived stress, contributing to mental disorders [9,14].

In addition to its psychological impact, childhood trauma affects the activity of the hypothalamic-pituitary-adrenal (HPA) axis and alters the levels of cortisol, a stress hormone released during HPA axis activation [15]. Childhood trauma often occurs during sensitive developmental periods, such as adolescence, when cortisol levels naturally increase and the HPA axis is particularly sensitive to stress [16,17]. Therefore, exposure to childhood trauma can overwhelm the developing stress-response system, leading to long-term dysregulation of HPA axis activity that may persist into adulthood, increasing vulnerability to chronic stress and the risk of mental disorders [17,18].

Hair cortisol concentration (HCC) is used to measure long-term cortisol levels [12,19,20]. In contrast to cortisol measurements from the serum, saliva, or urine[21], which can be affected by short-term fluctuations in cortisol secretion[22], HCC provides a time-averaged assessment over several months as cortisol accumulates in growing hair [23]. Thus, HCC is a reliable indicator of long-term HPA axis activity and is useful for investigating the influence of childhood trauma on physiological stress response. However, previous studies have reported inconsistent results. One study found an association between childhood trauma and lower HCC [24], while others found no association [12,25]. Meanwhile, one study observed a sex-specific effect, showing elevated HCC levels in women with greater childhood trauma exposure [26]. These inconsistencies suggest that other factors, such as sex differences and genetic predisposition [27,28] may influence the relationship between childhood trauma and HCC.

Gene-environment (G × E) interactions suggest that childhood trauma, as an environmental factor, can interact with genetic factors to influence biological mechanisms[29,30] and the development of mental disorders[31,32]. Among the candidate genes sensitive to psychological stress, the brain-derived neurotrophic factor (BDNF) gene influences the HPA axis through the production of BDNF [33]. The BDNF protein promotes the survival, growth, and maintenance of neurons [33,34], which are crucial for brain regions such as the hippocampus and prefrontal cortex [35], both of which are involved in regulating the HPA axis [36,37]. The BDNF Val66Met (rs6265) polymorphism is the most widely studied single nucleotide polymorphism (SNP) of the BDNF gene, leading to an amino acid substitution in which valine (Val) is replaced by methionine (Met) at codon 66 [38]. The Met allele exhibits less BDNF gene activity than Val homozygotes [38,39] and has been linked to higher cortisol levels in patients with depression [40], suggesting its potential influence on HPA axis activity. A study of veterans with PTSD [29] found that childhood trauma interacts with the BDNF Val66Met, particularly in Met carriers, leading to a blunted psychophysiological response to acute stress. This indicates that the interaction between BDNF Val66Met and childhood trauma affects stress responses. However, the effects of childhood trauma × BDNF Val66Met interactions on long-term HPA axis activity, such as in HCC, remain unclear, although it has been suggested that Met carriers with childhood trauma may experience reduced hippocampal volume [41–43], potentially leading to prolonged HPA activation [36] and higher allostatic load [44] over time, which may result in elevated HCC levels [45].

Notably, sex may play a crucial role in shaping the interactions between childhood trauma, the BDNF Val66Met genotype, and physiological stress responses. First, sex differences exist in childhood trauma exposure, with strong evidence showing that females often report higher levels of childhood trauma than males [29,46]. Second, sex differences were observed in HCC levels, although the findings were mixed. Some studies have shown that men have higher HCC levels[2,47], while another study reported higher HCC levels in girls [48], others have found no link with sex[45,49]. Third, sex differences also affect how the BDNF Val66Met variant influences HPA axis activity, with most studies focusing on salivary cortisol responses to acute psychological stress and showing mixed results. [26,50,51]. Finally, sex may influence the interaction between early life stress and the BDNF Val66Met on HCC levels. For example, one study found that higher neonatal pain-related stress predicted lower HCC levels in boys carrying the Met allele [28]. However, few studies have examined the interactive effects of childhood trauma × BDNF Val66Met × sex on long-term cortisol levels in adults, leaving a gap in the understanding of these complex interactions.

To address this gap, the author examined the relationship between childhood trauma and psychological and physiological responses to stress in healthy young adults. Regarding psychological responses, the association between childhood trauma and perceived stress was investigated, with the expectation that childhood trauma would be associated with higher levels of perceived stress. Given the limited evidence on how BDNF Val66Met and sex

influence the relationship between childhood trauma and perceived stress, the interaction effects were examined on an exploratory basis only. For physiological responses, the relationship between childhood trauma and HCC was examined based on the hypothesis that childhood trauma is linked to elevated HCC levels. The author also investigated the interaction between childhood trauma and the BDNF Val66Met genotype and expected that Met carriers would show significantly altered HCC levels in response to childhood trauma compared with Val/Val carriers. Additionally, the hypothesis was extended to a three-way interaction between childhood trauma, BDNF Val66Met, and sex, suggesting that sex further modulates the impact of childhood trauma on HCC levels.

2 MATERIAL AND METHODS

2.1 Study Sample

Secondary data were obtained from a previously published cross-sectional study [52] conducted from November 2016 to July 2018. This study involved 191 Korean participants aged 19–30, recruited through online advertisements and recruitment posters. One participant was excluded due to missing test data, resulting in a final sample size of 190 participants. All participants were screened for psychiatric illnesses using the Structured Clinical Interview for DSM-IV Axis I Disorders (SCID-IV). Exclusion criteria were as follows: 1) past or current psychiatric disorder, 2) lifetime neurologic disorder, 3) head trauma history accompanied by loss of consciousness, 4) a medical or surgical condition requiring hospitalization, 5) hospital discharge in the past 6 months, 6) taking oral contraceptives and glucocorticoid medication, and 7) currently pregnant or breastfeeding. Written informed consent was obtained from all participants, using procedures approved by the Institutional Review Board (IRB) of the Severance Hospital of the Yonsei University Health System (IRB No.2014-1767-035).

2.2 Psychological Measures

2.2.1 The Childhood Trauma Questionnaire (CTQ)

The CTQ [53] is a widely used screening tool for detecting childhood trauma including neglect and abuse [54]. It includes five subscales that evaluate different aspects of childhood trauma: emotional abuse, physical abuse, sexual abuse, emotional neglect, and physical neglect. CTQ scores can be interpreted by calculating the total score, with higher values reflecting greater levels of childhood trauma [55]. This approach is widely accepted and commonly used in research [54]. The internal consistency of CTQ in this study was 0.717.

2.2.2 The Perceived Stress Scale (PSS)

The PSS [56] is the most widely used psychological tool for evaluating an individual's perception of stress over the past month. Higher PSS scores indicate greater levels of negative distress and poorer positive coping abilities [57]. The ten-item Korean version of the PSS [58] has demonstrated reliability and validity (score range: 10–50) and was therefore used in this study. The internal consistency of PSS in this study was 0.789.

2.3 Hair Cortisol Analysis

Hair cortisol levels were measured following the procedures detailed in the primary study [52]. In brief, 10 strands/10mg of hair were collected from each participant and cut near the scalp, with a 3 cm segment used to estimate cortisol concentration over the past three months [59]. Cortisol levels were quantified via enzyme-linked immunosorbent assay

(ELISA), expressed as the cortisol-to-protein ratio (pg hair cortisol/μg hair protein). For further methodological details, please refer to the primary study [52].

2.4 Val66Met Genotyping

Genotyping of Val66Met (rs6265) was performed by Macrogen, Inc. using standard PCR amplification and Sanger sequencing methods as described in the primary study [52]. Based on the results of the analysis, genotype carriers were divided into two groups: Met allele carriers and Val/Val carriers. Full genotyping procedures are available in the primary publication [52].

2.5 Statistical Analysis

Statistical analyses were performed using SPSS (version 25, IBM, Chicago, IL, USA) and R software (https://www.r-project.org/). Participants were divided into two BDNF Val66Met genotype groups (Val/Val and Met carriers) and men and women groups and then tested for demographic characteristics. Bivariate associations among the study variables were examined using Pearson's correlation, and t-tests. To approximate a normal distribution, HCC levels were log-transformed, and BDNF Val66Met genotypes and sex were transformed into dummy variables for further analysis. The CTQ scores were calculated as the total scores to reflect overall trauma exposure.

To examine the association between PSS and CTQ score and further explore the potential effects of the Val66Met genotype and sex, a hierarchical linear regression model was performed. In this model, Step 1 included the main effects of CTQ score, the BDNF Val66Met genotype, and sex on PSS scores. In Step 2, the interaction term between CTQ score and the BDNF Val66Met genotype was added, and in Step 3, a three-way interaction term involving CTQ score, the BDNF Val66Met genotype, and sex was included.

To assess the relationship between HCC and CTQ score, along with the interaction effects of BDNF Val66Met and sex, a similar hierarchical linear regression model was applied. Step 1 included the main effects of CTQ scores, the BDNF Val66Met genotype, and sex on HCC. Step 2 added the interaction term for CTQ score and the BDNF Val66Met genotype, whereas Step 3 included the three-way interaction of CTQ score, the BDNF Val66Met genotype, and sex. To further investigate the associations between CTQ score and HCC within specific groups, separate linear regression analyses were conducted for four subgroups: women Val/Val, women Met, men Val/Val, and men Met carriers. A two-tailed significance level of 0.05 was applied to determine statistical significance.

3 RESULTS

3.1 Study Participants

The demographic characteristics, CTQ and PSS scores, and HCC levels of the 190 healthy, young participants are presented in Table 1. Data are provided for the total sample and stratified by Val66Met genotypes (Val/Val carriers versus Met carriers) and sex. There were no significant differences in sex distribution, CTQ scores, PSS scores, or HCC levels between the BDNF Val/Val and Met carriers. The BDNF Val66Met genotype distribution did not differ significantly from Hardy–Weinberg expectations ($\chi^2 = 0.14$, $p = 0.93$). Sex differences were observed in terms of age ($p = 0.036$) and years of education ($p = 0.043$), with men being older and having fewer years of education, likely due to mandatory military service requirements. However, age and education were not controlled in the following analysis because they are contextual factors that are not directly related to the study variables. In addition, there was no significant relation between HCC and PSS ($p = 0.829$).

Table 1 Demographic characteristics and CTQ, PSS score by Val66Met genotype and by sex

	Total (n= 190)	**Val/Val (n= 59)**	**Val/Met or Met/Met (n= 131)**	***p***	**Women (n=96)**	**Men (n=95)**	***p***
Age, mean (SD), years	23.0 (2.6)	23.0 (2.5)	23.0 (2.6)	0.873	22.6 (2.6)	23.4 (2.6)	0.036
Sex, N(%)				0.074			
Female	96 (50.5)	36 (61.0)	60 (45.8)				
Male	94 (49.5)	23 (39.0)	71 (54.2)				
Education, mean (SD), years	14.4 (1.4)	14.3 (1.4)	14.4 (1.4)	0.702	14.6 (1.5)	14.2 (1.3)	0.043
CTQ, mean (SD)	37.6 (10.1)	37.7 (9.9)	37.6 (10.3)	0.939	37.2 (9.8)	38.0 (10.5)	0.575
PSS, mean (SD)	25.7 (5.5)	26.2 (5.6)	25.4 (5.4)	0.366	26.0 (5.4)	25.3 (5.6)	0.379
HCC, median(IQR), pg /μg	5321.8 (6014.9)	5399.8 (6870.3)	5112.7 (5602.7)	0.243	8923.8 (6039.1)	5768.6 (5943.8)	0.061

Note: Sex and BDNF Val66Met genotypes were entered as dummy variables (men=0, women=1; Val/Val carriers=0, Met carriers=1). Abbreviations: CTQ, the Childhood Trauma Questionnaire; PSS, the Perceived Stress Test; HCC, hair cortisol concentration.

3.2 Associations of Childhood Trauma with Perceived Stress

Hierarchical linear regression analysis showed that PSS scores were positively related to CTQ scores (B = 0.124, $p = 0.002$; Step 1). For exploratory purposes, there were no interactions of CTQ score × BDNF Val66Met ($p = 0.712$; Step 2) or CTQ score × BDNF Val66Met × sex ($p = 0.081$; Step 3) with PSS score. The detailed regression model results are presented in Table 2, and the association between the CTQ and PSS scores is illustrated in Figure 1.

Table 2 Hierarchical linear regression model of PSS score with CTQ score, Val66Met genotype, and sex

		PSS Score		
		B	**95% CI**	***p***
Step 1	CTQ Score	0.124	[0.048, 0.200]	0.002
	BDNF Val66Met	-0.670	[-2.349, 1.008]	0.431
	Sex	0.720	[-0.835, 2.275]	0.362
Step 2	CTQ Score × BDNF Val66Met	-0.032	[-0.200, 0.137]	0.712
Step 3	CTQ Score × BDNF Val66Met × Sex	0.302	[-0.038, 0.640]	0.081

Note: Sex and BDNF Val66Met genotypes were entered as dummy variables (men=0, women=1; Val/Val carriers=0, Met carriers=1). Abbreviations: CI, confidence interval, CTQ, the Childhood Trauma Questionnaire; PSS, the Perceived Stress Scale.

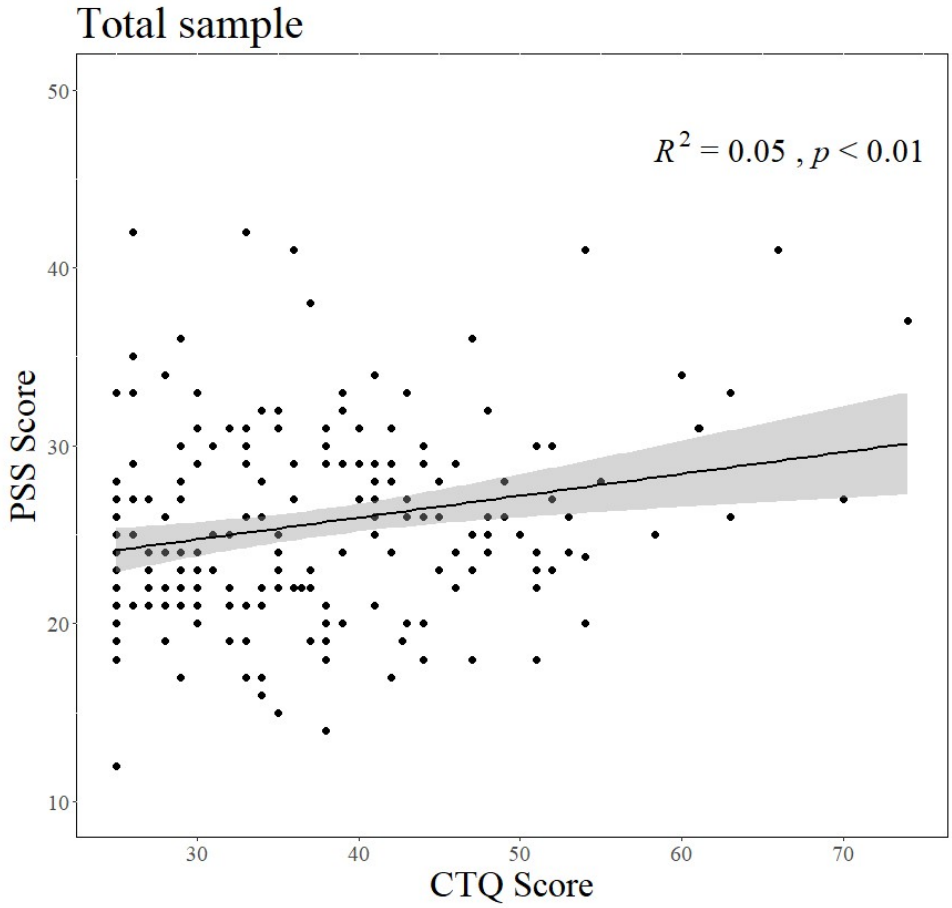

Figure 1 Association of CTQ score with PSS score in total sample
Note: The line in the scatter plot represents the simple linear regression line. The shaded area indicates the 95% confidence interval. R^2 value represents the strength of this relationship. Abbreviations: CTQ, the Childhood Trauma Questionnaire; PSS, the Perceived Stress Scale.

3.3 Associations of Childhood Trauma, BDNF Val66Met Genotype, and Sex with HCC

The results of the hierarchical linear regression model are presented in Table 3. In Step 1, no significant main effect of CTQ score on HCC was found in the total sample (p= 0.452). Similarly, there were no significant associations of HCC with BDNF Val66Met genotype (p = 0.626) and sex (p = 0.075). In Step 2, the interaction effect of CTQ score and BDNF Val66Met genotype on HCC was not significant (p = 0.593). In Step 3, the three-way interaction among CTQ score, BDNF Val66Met genotype, and sex showed a significant association with HCC (p = 0.014), although the overall model did not reach statistical significance ($F_{7,182}$=1.859, p=0.089).

To further investigate sex and Val66Met genotype differences, the sample was divided into four groups: Men Val/Val carriers (n = 23), Men Met carriers (n = 71), Women Val/Val carriers (n = 36), and Women Met carriers (n = 60). As shown in Table 4 and Figure 2, a positive association between HCC and CTQ score was observed exclusively in women Val/Val carriers (B=0.019, p=0.034), with no significant association in the other three groups (all p value> 0.101).

Table 3 Hierarchical linear regression model of HCC with CTQ score, Val66Met genotype, and sex

		HCC level		
		B	**95% CI**	***p***
Step 1	CTQ Score	0.002	[-0.003, 0.007]	0.452
	BDNF Val66Met	-0.028	[-0.141, 0.085]	0.626
	Sex	0.095	[-0.010, 0.199]	0.075
Step 2	CTQ Score × BDNF Val66Met	-0.003	[-0.014, 0.008]	0.593
Step 3	CTQ Score × BDNF Val66Met × Sex	-0.028	[-0.051, -0.006]	0.014

Note: Sex and BDNF Val66Met genotypes were entered as dummy variables in total sample analysis. Abbreviations: CI, confidence interval, CTQ, the Childhood Trauma Questionnaire; HCC hair cortisol concentration.

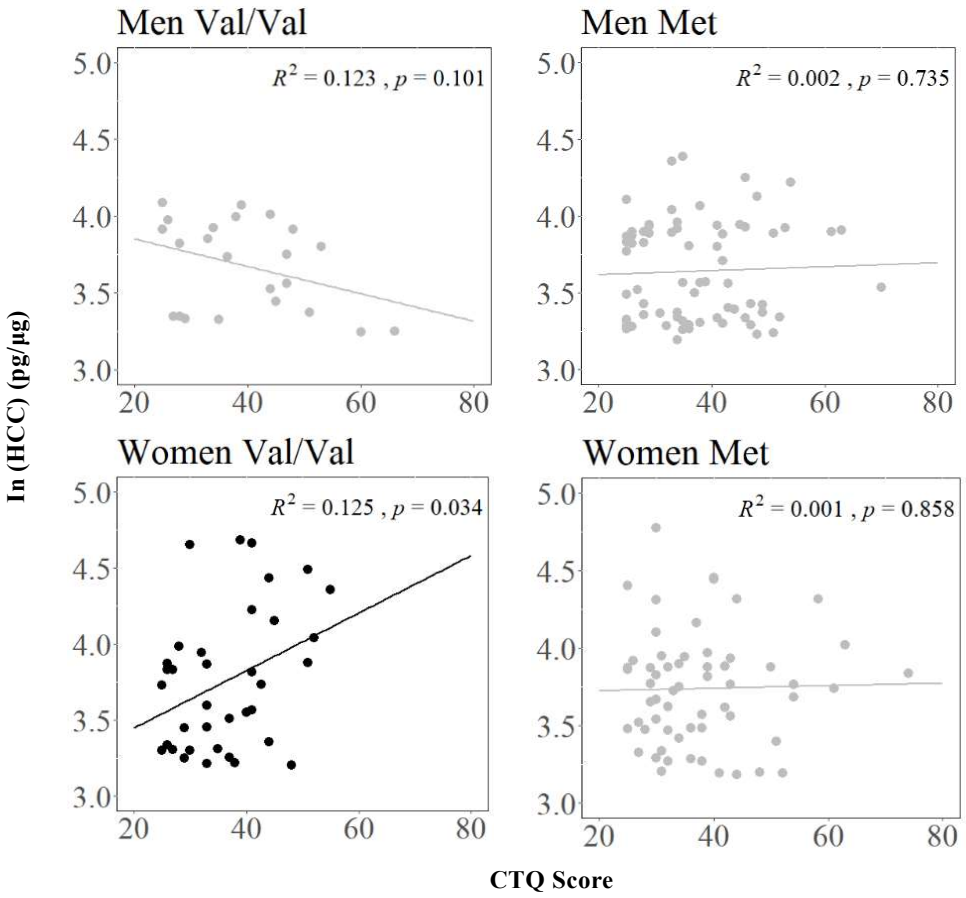

Figure 2 Association of HCC with CTQ score in groups divided by sex and Val66Met genotype.
Note: Y-axis, hair cortisol values calculated by cortisol-to-protein ratio (pg hair cortisol/μg hair protein) and then transformed into natural log values, X-axis, CTQ score; the line in the scatter plot represents the simple linear regression line. R^2 value represents the strength of this relationship. Abbreviations: CTQ, the Childhood Trauma Questionnaire; HCC, hair cortisol concentration.

4 DISCUSSION

This study examined the relationship between childhood trauma and psychological and physiological stress responses among healthy young adults, considering the effects of the BDNF Val66Met genotype and sex differences. Regarding psychological stress responses, higher exposure to childhood trauma was associated with increased perceived stress across all participants, regardless of sex or Val66Met genotype. Regarding physiological stress responses, the results partially supported the hypothesis regarding the interactions between childhood trauma, the BDNF Val66Met genotype, and sex. While no significant main effect of childhood trauma on HCC was found in the total sample, nor was there a significant two-way interaction between childhood trauma and the BDNF Val66Met genotype, a three-way interaction between childhood trauma and BDNF Val66Met × sex was observed. Specifically, in female Val/Val carriers, greater childhood trauma was associated with elevated HCC. Meanwhile, no significant association between childhood trauma and HCC was found in men of either genotype or in women with the Met allele. Overall, childhood trauma significantly influenced psychological responses and the interaction of childhood trauma × BDNF Val66Met × sex influenced physiological responses. Notably, a strong effect was observed in women with the Val/Val genotype, highlighting the importance of these interactions in long-term stress regulation.

Regarding perceived stress, childhood trauma was positively associated with perceived stress across all participants. This finding aligns with previous research [12,26,60,61], highlighting the strong relationship between childhood trauma and stress perception. According to the PSS questionnaire [50,62], high levels of perceived stress reflect both increased negative distress and poor coping abilities. This suggests that individuals with greater childhood trauma may not only feel overwhelmed by stress but also have more difficulty coping effectively, which may result in more psychological stress. Given that elevated levels of perceived stress are associated with various mental health conditions such as depression [63] and anxiety [8], childhood trauma may contribute to the development of psychopathology by increasing perceived stress. In addition, no significant interaction between childhood trauma and the BDNF Val66Met genotype or a three-way interaction with sex was observed for perceived stress, suggesting that childhood trauma independently contributes to perceived stress without interacting with the Val66Met genotype and sex.

Regarding HCC in relation to childhood trauma, there was no main association between childhood trauma and HCC. This result aligns with several previous studies showing non-significant results [12,25,64], while other studies have reported significant associations [24,26]. This suggests that factors such as BDNF Val66Met genotype and sex, as examined in this study, may contribute to the complex relationship between childhood trauma and HCC.

Regarding HCC in relation to the two-way interaction of childhood trauma with the BDNF

Val66Met genotype, no significant interaction effect on long-term HPA axis activity was found. However, this result contradicts the previous hypothesis that Met carriers exposed to childhood trauma have higher HCC levels. The non-significant results of this study suggest that more complex mechanisms may underlie this relationship, potentially influenced by other factors such as sex. Sex differences, in particular, may dilute the impact of this interaction on physiological stress responses, as the author observed a complicated three-way interaction involving sex.

Regarding HCC in relation to the three-way interaction of sex, childhood trauma, and the BDNF Val66Met genotype, a positive association between HCC and childhood trauma was found exclusively in women with the Val/Val genotype. This suggests that women with the Val/Val genotype may experience the most pronounced impact of childhood trauma on long-term cortisol response, compared to other sex and genotype groups.

A possible explanation may lie in the combined interactions of sex with the BDNF Val66Met genotype, and sex with childhood trauma, which together may influence HPA reactivity to acute stress and relate to HCC levels [65]. In terms of sex and the BDNF Val66Met interaction, previous research in the general population suggests that women Val/Val carriers tend to exhibit lower cortisol responses to acute stress, such as the Trier Social Stress Test (TSST), whereas Val/Val men demonstrate higher acute cortisol reactivity [66,67]. This indicates that women Val/Val carriers exhibit impaired HPA reactivity. In terms of sex and childhood trauma interaction, previous research in the general population found that women with childhood trauma exhibited blunted cortisol responses to acute stress (the TSST) [68], further suggesting impaired HPA reactivity in this group. Furthermore, previous research has shown that HPA reactivity is associated with HCC levels, with healthy individuals with higher HCC exhibiting lower cortisol reactivity to acute stress [65].

In summary, these findings suggest that women Val/Val carriers with childhood trauma may experience impaired HPA reactivity, which may also have contributed to the elevated HCC levels observed in this study [65]. Therefore, a potential shift from resilience via acute reactivity to vulnerability through chronic allostatic loading in the HPA axis [44,69] may exist in women Val/Val carriers with childhood trauma, which leads to impaired HPA reactivity over time and elevated long-term HPA axis activity [65,70].

This study has several limitations. First, the nature of the secondary data imposes constraints, as the original study [52] was not specifically designed to address the current research questions. The data included only HCC levels, which represent long-term HPA activity, and did not measure cortisol reactivity to acute stress. Therefore, these results may not provide a complete picture of how cortisol responses and reactivity are affected by childhood trauma, sex, and BDNF Val66Met genotype and their interactions. Additionally, the modest sample size may have led to less stable estimates of the associations, underscoring the need for replication with larger samples to confirm these findings. Second, the reliance on subjective self-reported questionnaires, such as the CTQ and PSS, to assess psychological measures introduces

potential bias and complicates the analysis of their relationship with HCC, which is an objective physiological measure. Third, the sample consisted exclusively of healthy young adults without mental disorders, which may not generalize to other age groups or individuals with mental health conditions. Future studies should address these limitations by including more diverse populations. Finally, confounders may exist and affect the evaluation of HCC levels, as HCC may be influenced by external factors such as hair washing frequency, hair treatments, and BMI [59,71,72], which were not fully controlled in this study.

5 CONCLUSION

In summary, the findings suggest a positive relationship between childhood trauma and perceived stress, as well as a three-way interaction of childhood trauma × BDNF Val66Met × sex in long-term HPA axis regulation. Specifically, a positive association between childhood trauma and HCC was observed only in women Val/Val carriers, indicating that this subgroup might experience a more pronounced long-term physiological response influenced by childhood trauma. This unique interaction pattern of interaction suggests that genetic factors (BDNF Val66Met), environmental factors (childhood trauma), and sex may interact to play crucial roles in shaping chronic physiological responses to stress. Future research should explore the mechanisms underlying these interactions and include diverse clinical samples to better understand their implications on mental health.

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ABSTRACT IN KOREAN

아동기 외상이 스트레스지각 및 모발 코티졸 수준에 미치는 영향: BDNF Val66Met 유전자형과 성별에 따른 차이

아동기 외상은 스트레스지각과 장기 HPA 축 활동을 포함하는 성인기 스트레스의 심리 및 생리 반응에 영향을 미침으로써 정신 장애의 위험을 증가시킨다. 이 효과의 기저에는 뇌유래신경영양인자(BDNF) Val66Met 다형성과 성별이 중요한 역할을 하는 유전자-환경(G × E) 상호작용이 작동할 수 있다. 저자는 BDNF Val66Met 다형성과 성별 차이를 고려하여 아동기 외상이 스트레스 반응에 미치는 영향을 조사하고자 하였다.

190명의 건강한 젊은 성인(여성 96명)을 대상으로 이차 자료를 분석하였다. 아동기 외상은 아동기외상설문(CTQ)을, 스트레스지각은 지각된 스트레스척도(PSS)를 사용하여 측정하였으며, 장기 코티졸 수준은 모발코티졸농도(HCC)를 지표로 사용하였다. 참가자들은 BDNF Val66Met 다형성에 대한 유전자형 분석을 통해 Val/Val과 Met 보유자로 구분하였다. CTQ 점수, BDNF Val66Met 유전자형 및 성별 사이의 상호작용이 PSS 점수와 HCC에 미치는 영향을 평가하기 위해 계층선형회귀모델을 사용하여 분석하였다. 추가 분석에서는 성별에 따라 Val/Val 및 Met 보유자에 대한 별도의 선형회귀모델을 실시하였다.

전체 참가자에서 CTQ 점수가 높을수록 PSS 점수 역시 높아지는 유의한 상관관계가 나타났다. HCC에 대해서는 CTQ 점수, BDNF Val66Met 유전자형 또는 성별의 유의한 주효과는 관찰되지 않았다. 그러나 HCC에 대해 여성 Val/Val 보유자에서만 HCC와 아동기외상 사이에 유의한 양의 상관관계가 나타나는 CTQ 점수, BDNF Val66Met 및 성별 사이의 유의한 삼원 상호작용이 관찰되었다.

이 연구는 아동기 외상이 모든 참가자의 스트레스지각을 증가시키고, 여성 Val/Val 보유자에서만 HCC 수치를 증가시킨다는 점을 보여주어 아동기 외상, BDNF Val66Met 및 성별이 스트레스 반응을 형성하는 데 중요한 역할을 함을 강조한다. 이 소견은 아동기 외상이 HPA 축에 미치는 장기적인 영향을 연구할 때 유전자 및 성별 요인을 고려하는 것이 중요하다는 점을 시사한다. 향후 연구에서는 좀 더 다양한 나이 및 임상조건이 있는 집단에서 이 상호작용의 기저 기전을 밝힐 필요가 있다.

핵심되는 말 : 뇌유래신경영양인자, Val66Met, 아동기 외상, 스트레스, 모발코티졸