



Perceived Stress Mediates the Relationship Between Childhood Trauma and Onset of Bruxism Among Adolescents

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Purpose: Bruxism is relatively common among adolescents; however, the psychological factors affecting its occurrence remain unclear. This study explored the incidence of bruxism in adolescents, and the role of childhood trauma and perceived stress in the occurrence of bruxism.

Patients and Methods: This was an online cross-sectional survey of 7794 adolescents aged 12–18 years, with 6780 adolescents meeting the inclusion criteria. We used the Adverse Childhood Experiences Questionnaire (ACEQ) to assess childhood trauma experiences, the Perceived Stress Scale (PSS) to evaluate stress in adolescents, and three items to assess bruxism. The chi-square test was used for demographic data and *t*-test was used for continuous variables. A mediation analysis was used to explore the mechanism of childhood trauma as it relates to bruxism.

Results: Our research shows that about 21.6% of sampled adolescents had bruxism. Being in adolescents, childhood trauma, and high levels of perceived stress were risk factors for bruxism, and good academic performance was a protective factor against bruxism. Adolescents with bruxism had higher levels of childhood trauma and perceived stress. Perceived stress levels played a mediating role in the relationship between childhood trauma and the development of bruxism.

Conclusion: Bruxism is common in adolescents, and its occurrence is related to childhood trauma and perceived stress levels. Childhood trauma mediates bruxism through perceived stress levels. Attention should be paid to the childhood trauma experiences and perceived stress levels of adolescents with bruxism, and timely interventions should be provided that are conducive to reducing the occurrence of bruxism.

Keywords: bruxism, childhood trauma, perceived stress, adolescents

Introduction

Bruxism is the repetitive movement of the jaw muscle groups, characterized by clenching or grinding the teeth by pushing the lower jaw, to complete a non-functional movement. According to the different circadian rhythm characteristics of bruxism, it can be divided into awake bruxism (AB) and sleep bruxism (SB). According to the different rhythm states of molar movement, bruxism can be divided into grinding and clenching types.¹ Bruxism leads to dentin allergies, which can cause pulpitis in severe cases.² It can also cause the occlusal plane to decrease, induce or aggravate temporomandibular joint disease and temporomandibular joint disorder syndrome, and can also lead to broken teeth, oral trauma, facial paralysis, and headaches.^{3,4} In addition, sleep bruxism damages the nighttime sleep structure and reduces total sleep time, non-rapid eye movement (NREM) sleep latency, sleep efficiency, and sleep quality, while increasing rapid eye movement (REM) sleep time.⁵

Systematic reviews and meta-analyses show that the global incidence of bruxism (sleeping and waking) among adults is 22.22%. There are regional differences in bruxism. The incidence of sleeping bruxism is the highest in North America at 31%, and the lowest in Asia at 19%. For waking bruxism, North America also has the highest incidence at 30%, followed by Asia at 25%.⁶ Studies on adolescents have found that the incidence of sleep bruxism was basically similar to adults, approximately 31%, but the incidence of awake bruxism is 51.6%.⁷ Geographical environmental factors are

closely related to the occurrence of bruxism. Climate and seasonality, socio-economic status, living environment, areas with high intake of caffeine, alcohol and tobacco all have an impact on bruxism.^{8–12} For instance, research shows that there is a global trend of seasonal bruxism, which is characterized by a significant increase in winter and a decrease in summer.¹³ There are relatively few studies on bruxism among teenagers in China, only in 2011, Wan et al investigated the incidence of SB among adolescents in eastern Henan Province; thus, more recent, largescale surveys on the incidence of SB and AB among Chinese adolescents are lacking.¹⁴

The pathogenesis of bruxism is unclear; it may be caused by multiple factors such as maxillary relationship disorder,¹⁵ maxillofacial bone malformation, pathophysiological factors, and genetic factors;¹⁶ increasingly, attention is being given to mental and psychological factors. Studies have shown that bruxism is closely associated with various stress factors. State anxiety, trait anxiety, alexithymia, and perceptual stress are as important as physical factors in the occurrence and maintenance of AB.¹⁷ A study of 2089 college students in Brazil using the Stress Perception Scale found that students with high stress levels or depression had a higher prevalence of SB than those without any symptoms, and that SB was more prominent in female students.¹⁸ Another study on SB found that perceived stress scores were associated with the use of bruxoff devices to record the molar index at night, with the higher the score, the higher the bruxism index.¹⁹ However, current research on the relationship between perceived stress and bruxism mainly focuses on college students and adults; there is a lack of research on adolescents, and the results are inconsistent. Some studies have not found a relationship between perceived stress and bruxism.^{20,21}

Several studies have investigated the relationship between childhood trauma and bruxism.^{22–24} Total childhood trauma scores were significantly higher in patients with bruxism than in those without bruxism.²⁵ A systematic review showed that parental relationship dissolution, the most common childhood traumatic experience, can impact children's sleep, causing problems such as sleep bruxism, nightmares, and enuresis.²⁶ Other studies have shown that adverse childhood traumatic experiences such as low socioeconomic status²⁷ and verbal school bullying can significantly increase the incidence of bruxism among schoolchildren and adolescents.²⁸ However, current research on the effects of childhood trauma on bruxism has been inconsistent and even contrary.^{29,30}

Recently, the relationship between childhood trauma and stress perception has received increasing attention. Both cross-sectional and cohort studies have found higher levels of perceived stress among adolescents with trauma childhood experiences.^{31,32} Studies of adolescents and young adults in China have found that childhood trauma can mediate suicidal ideation and risky behaviors through perceived stress levels.^{33,34} Research has also indicated that the effects of childhood trauma on sleep disorders, especially insomnia symptoms, may be related to increased perceived stress.³⁵ Unfortunately, no studies have explored the relationships between childhood trauma, perceived stress, and bruxism in adolescents. The present study focused on the incidence of bruxism in Chinese adolescents and its related influencing factors, as well as the relationships between bruxism, childhood trauma, and perceived stress. We hypothesized that the occurrence of bruxism is mediated by increased perceived stress levels during childhood.

Material and Methods

Study Population and Design

This study used an online cross-sectional survey of junior and senior high school students aged 12–18 years old. We used the Wenjuanxing platform (<https://www.wjx.cn/app/survey.aspx>) to assess bruxism and its related influencing factors in adolescents from May 1 to May 30, 2022. The participants were mainly from Shandong Province, and cluster sampling was adopted according to class. A psychology teacher distributed the questionnaire through WeChat and QQ. The students were required to read the guidance carefully and give answers according to the requirements. A total of 7734 participants participated in the survey, excluding incomplete questionnaires, which were completed by 6780 adolescents. The effective response rate was 87.6%. The selection criteria were as follows: (1) junior and senior school students, (2) able to read and understand Chinese questionnaires, (3) QQ users or WeChat, (4) voluntary participation in the investigation. The exclusion criteria were as follows: (1) participants who did not complete their answers and (2) participants who Answer freely or within 5 minutes.

This study was approved by the Medical Ethics Committee of Beijing Huilongguan Hospital (Approval No. 2021–18-Department). Before the investigation, electronic informed consent was signed by and obtained from the students and their guardians.

Assessment Tools and Procedure

Sociodemographic Factors

The demographics collected included sex, age, grade level, whether the children were left behind, and academic performance.

Bruxism

To evaluate the occurrence of bruxism in adolescents in the past month, the following three questions about bruxism, modified from Van der Meulen et al³⁶ were asked: In the past month, have you ever been told or have you noticed that you grind your teeth while sleeping? Have you ever woken up in the morning or during the night with a squeezing or tensing sensation in your jaw? Have you talked in your sleep in the past month?

Adverse Childhood Experiences

The revised version of the Adverse Childhood Experiences Questionnaire (ACEQ-R) was used to assess adverse childhood experiences among adolescents. The ACEQ-R is a relatively comprehensive tool for studying adverse childhood experiences. Finkelhor et al added four items based on the original ACEQ, totaling 14 items.³⁷ The scale measures whether participants have experienced any of the adverse experiences before the age of 18. The scores of the 14 items on the scale are summed to obtain the individual's total ACEQ-R score. The higher the total score, the more types of adverse experiences they have accumulated. The revised version of the Chinese Adverse Childhood Experience Questionnaire was introduced and revised by Cao et al and tested for reliability and validity.³⁸ Three factors including “childhood abuse and neglect”, “family dysfunction”, and “other adversity” were included. The K-R20 series number was 0.83, and Guttman's split-half reliability coefficient r was 0.75.

Perceived Stress

The Perceived Stress Scale (PSS) was used to evaluate adolescent stress perceptions.³⁹ We obtained the license (113766) from Mapi Research Trust. The PSS is one of the most commonly used research tools for measuring individuals' perceived stress levels at home and abroad. The tool not only measures the level of stress that an individual is currently experiencing but also assesses whether the external pressure exceeds the individual's ability to cope, mainly looking at the degree of stress an individual has experienced in daily life in the last month due to unpredictable, uncontrollable, or overburdened stress. In this study, a 10-item short-form scale (PSS-10) was used, and a Likert rating scale of 0–4 was adopted, with a total score of 0–40; the higher the score, the more severe the perceived stress. The results show that the Chinese version of the PSS-10 has good reliability and validity.⁴⁰

Statistical Analysis

We used SPSS26 software (version SPSS 26.0) for data analysis. The chi-square test was used to compare categorical variables in the demographic data, and percentages were used to represent the proportion of molars in different demographic data. Mean \pm standard deviation comparison was used for continuous variables, and the effect size was represented by Phi/Cramer V. An independent sample t -test was used to measure the differences in childhood trauma and perceived stress between bruxism and non-bruxism groups, and the effect size was represented by Cohen's d . A Pearson's correlation analysis was performed to explore the correlation between childhood trauma and perceived stress. Binary logistic analysis was used to explore the factors related to adolescent bruxism, and the effect size was represented by Cohen's d . Bilateral $p < 0.05$ indicates statistical significance. In addition, G*Power 3.1.9.7 has been used to calculate the power of chi-square test, binary logistic regression, independent sample t -test and Pearson's correlation analysis. The results indicated that their sizes were 0.90–1.00, and the sample size was sufficient to detect even small effects according to the latest guidelines.⁴¹

We adopted SPSS AU for mediation analysis (<https://spssau.com/>), and the mediating effects model used the scores of childhood maltreatment, household dysfunction, other adversity, and ACEQ-R total score as the predictor, the groups with or without bruxism were used as the outcome measure, and total score of perceived pressure total score was used as the mediation factor. Bootstrap method was used to explore the mediation effect of perceived stress between childhood trauma and bruxism. The sample size was 5000 and 95% confidence interval was adopted. The 95% CI of the indirect effect does not include zero, indicating that the mediation effect is established.

Results

Socio-Demographic Characteristics and Association with Bruxism

A total of 6780 adolescents meeting the research criteria were included in this study, including 3163 males (46.7%) and 3617 females (53.4%), with a mean age of 15.90 ± 1.44 years old. A total of 1479 adolescents had bruxism, an incidence rate of 21.8%; the incidence of SB was 12.3%, the incidence of AB was 5.0%, and the incidence of jaw clenching was 12.6%. The incidence of AB combined with AB was 2.6%, that of AB combined with jaw clenching was 3.1%, and that of SB combined with jaw clenching was 4.7%. The total proportion of AB among male students was higher than that among female students ($p=0.001$). Except for AB, the proportions of SB, jaw clenching, and total teeth bruxism were higher in high school students than in middle school students (all $p<0.001$). The proportion of left-behind children with jaw clenching was higher than that of non-left-behind children ($p=0.040$). In terms of academic performance, the proportion of adolescents with poor academic performance in the incidences of AB, jaw clenching, and total bruxism was higher than that of students with medium or good academic performance (all $p<0.001$) (Table 1).

Differences in Adverse Childhood Experiences and Perceived Stress Between Adolescents with Bruxism and Those Without Bruxism

Adolescents with bruxism had significantly higher scores for childhood maltreatment ($t=12.14$, $p<0.001$), household dysfunction ($t=9.07$, $p<0.001$), other adversities ($t=10.67$, $p<0.001$), and ACEQ-R total scores ($t=13.33$, $p<0.001$) than those without bruxism. Perceptions of stress ($t=18.08$, $p<0.001$) and total perceived stress scores ($t=15.97$, $p<0.001$) were higher for adolescents with bruxism than for those without bruxism (Figure 1).

Relationship Between Adverse Childhood Experiences and Perceived Stress

There were positive correlations between childhood maltreatment, household dysfunction, other adversities, and ACEQ-R total score, perception of stress and total perceived stress ($r_s=0.118-0.890$, all $p<0.001$). There were negative correlations between the ability to cope with stress and childhood maltreatment, household dysfunction, other adversities, ACEQ-R total score, perception of stress and total perceived stress ($r_s=-0.044 - -0.546$, all $p<0.001$) (Figure 2).

Effects of Adverse Childhood Experiences, and Perceived Stress on Bruxism in Adolescents

Binary logic analysis showed that in terms of demographic data, being a senior high school was a risk factor for bruxism in adolescents compared with being in junior high school (odds ratio [OR]=1.31, 95% CI=1.15–1.48). Compared with bad academic performance, moderate (OR=0.86, 95% CI=0.75–0.98) and good academic performance (OR=0.74, 95% CI=0.63–0.86) were protective factors against bruxism in adolescents. For adverse childhood experiences, binary logistic regression showed that childhood maltreatment (OR=1.31, 95% CI=1.26–1.38), household dysfunction (OR=1.32, 95% CI=1.24–1.41), other adversities (OR=1.67, 95% CI=1.51–1.84), and ACEQ-R total score (OR=1.18, 95% CI=1.15–1.21) were the risk factors for bruxism in adolescents. We also observed that subjects' perception of stress (OR=1.10, 95% CI=1.09–1.12) and total perceived stress (OR=1.18, 95% CI=1.15–1.21) were risk factors for bruxism in adolescents (Table 2 and Supplementary Table 1).

Table 1 Socio-Demographic Characteristics and Association with Bruxism (N = 6780)

Variables	n	%	Sleep Bruxism				Jaw Clenching				Wake Bruxism				All Bruxism			
			n	%	P	Phi/Cramer V	n	%	P	Phi/Cramer V	n	%	P	Phi/Cramer V	n	%	P	Phi/Cramer V
Gender					0.121	-0.019			0.374	-0.011			0.001	-0.041			0.215	-0.015
Male	3163	46.7	410	13.0			411	13.0			208	6.6			711	22.5		
Female	3617	53.3	424	11.7			444	12.3			169	4.7			768	21.2		
Grade					0.005	0.034			<0.001	0.056			0.060	0.023			<0.001	0.051
Junior high school	2410	35.5	260	10.8			244	10.1			117	4.9			457	19.0		
Senior high school	4370	64.5	574	13.1			611	14.0			260	5.9			1022	23.4		
Left behind children					0.809	0.003			0.040	-0.025			0.889	-0.002			0.055	-0.023
Yes	1330	19.6	161	12.1			190	65.7			75	5.6			316	23.8		
No	5450	80.4	673	12.3			665	64.9			302	5.5			1163	21.3		
Exam results					0.093	0.026			<0.001	0.052			0.012	0.036			<0.001	0.051
Bad	2155	31.8	283	13.1 ^a			322	14.9 ^b			145	6.7 ^c			524	24.3 ^d		
Moderate	2863	42.2	359	12.5			349	12.2			150	5.2			618	21.6		
Good	1762	26.0	192	10.9			184	10.4			82	4.7			337	19.1		

Notes: a represents the difference in the incidence of sleep bruxism between bad and good exam results; b indicates that the incidence of jaw clenching for bad exam results was higher than that of adolescents with moderate and good exam results; c indicates that the incidence of wake bruxism for bad exam results was higher than that of adolescents with moderate and good exam results; d indicates that the incidence of bruxism among adolescents with poor academic performance is the highest, followed by those with medium academic performance, and the lowest among those with good academic performance, and it is statistically significant.

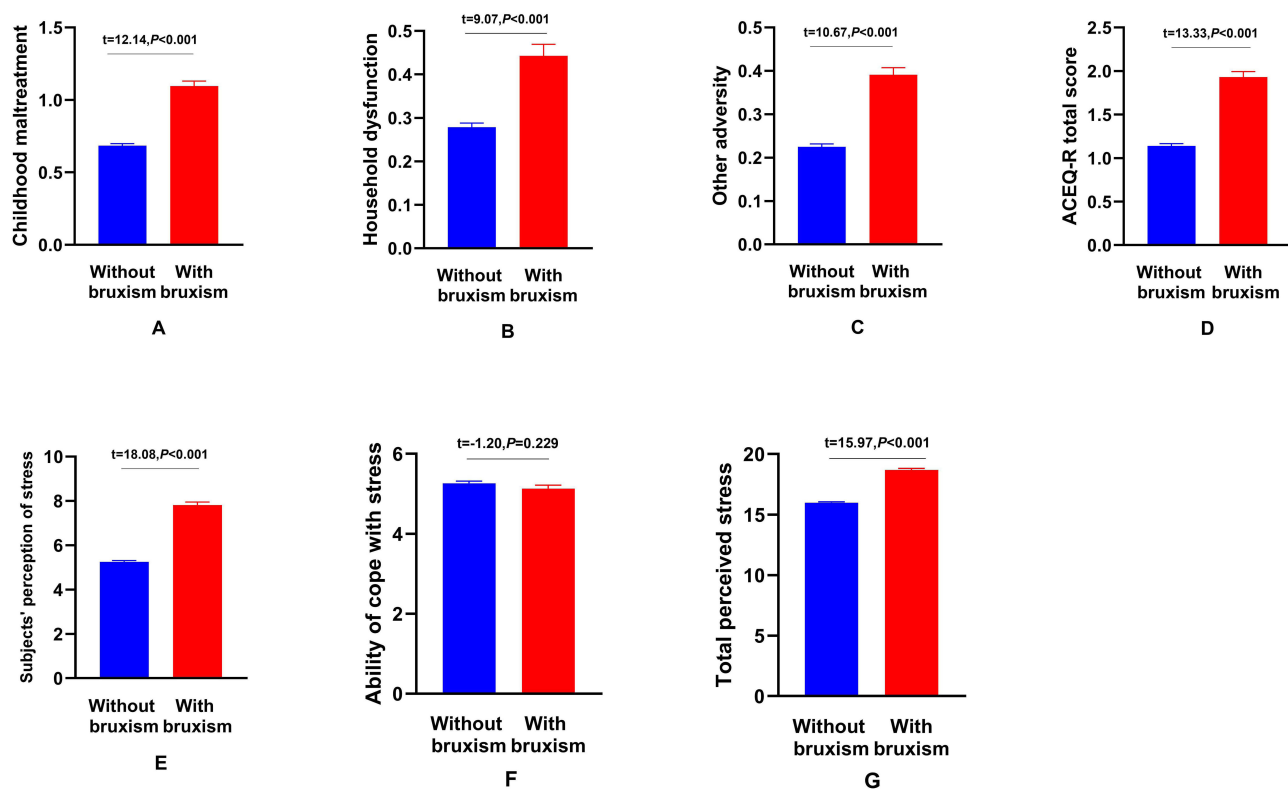


Figure 1 Differences in childhood trauma and perceived stress in adolescents with and without bruxism ($N = 6780$). **(A)** indicates that adolescents with bruxism exhibit significantly higher childhood maltreatment scores compared to those without bruxism; **(B)** indicates that adolescents with bruxism exhibit significantly higher household dysfunction scores compared to those without bruxism; **(C)** indicates that adolescents with bruxism exhibit significantly higher household dysfunction scores compared to those without bruxism; **(D)** indicates that adolescents with bruxism exhibit significantly ACEQ-R total scores compared to those without bruxism; **(E)** indicates that adolescents with bruxism exhibit significantly subjects' perception of stress scores compared to those without bruxism; **(F)** indicates that adolescents with bruxism exhibit significantly ability of cope with stress scores compared to those without bruxism; **(G)** indicates that adolescents with bruxism exhibit significantly total perceived stress compared to those without bruxism.

Mediation Analysis

Binary logistic regression suggests that childhood trauma and perceived stress are risk factors for adolescents' bruxism. We tested mediation effect models using ACEQ-R measures as predictors and bruxism diagnosis comparisons as outcome measures. Total perceived stress was used as the mediation factor for all models. Models 1–4 used childhood maltreatment, household dysfunction, other adversities, and ACEQ-R total score measures, the 95% CI for indirect effects did not include zero, suggesting that the mediation effect was statistically significant, suggesting that Models 1–4 were partial mediation models (Figure 3).

Discussion

Our study found a higher incidence of bruxism in adolescents, with childhood trauma and perceived stress scores being risk factors for bruxism. Childhood trauma mediated bruxism through perceived stress levels. Most importantly, we found that perceived stress levels mediated the relationship between childhood trauma and bruxism onset.

Currently, there are few studies on bruxism in Chinese adolescents. Our study found that the incidence of bruxism in adolescents is 21.8%, and previous studies have also shown that bruxism is the most common sleep problem among Chinese adolescents.^{42,43} Furthermore, our research found that the prevalence of bruxism among adolescents was basically consistent with that in the global meta-analysis. However, in this meta-analysis, it was discovered that the incidences of sleep bruxism and awake bruxism among Asian children were 14% and 22% respectively, which were higher than our research results.⁶ Our study found no significant gender differences in bruxism, with the exception of higher rates of AB in males compared to females. This is not completely consistent with the previous results, most of which found no gender differences between AB and SB^{44,45}, while only a few found that AB was more common in

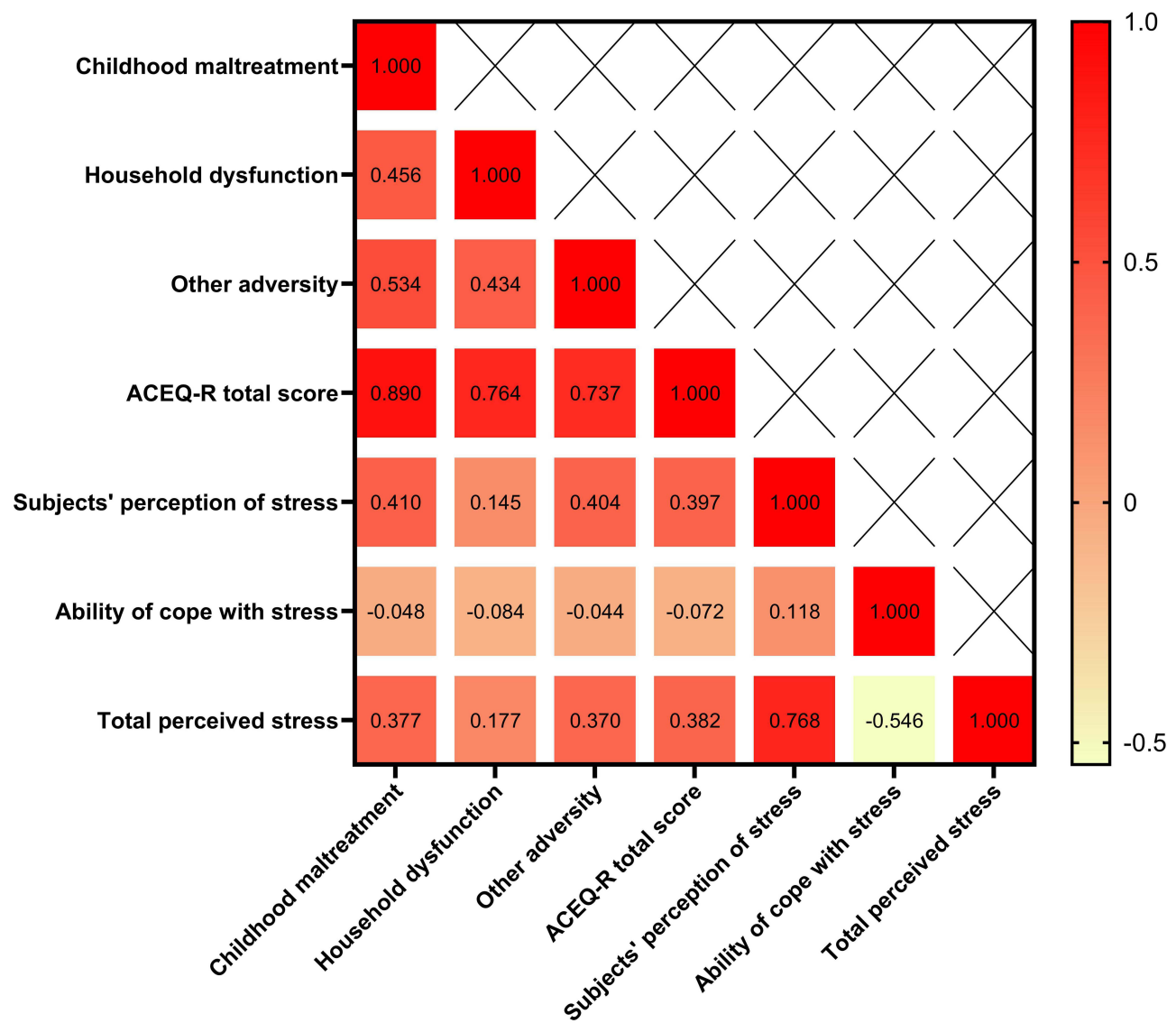


Figure 2 The correlation analysis between adverse childhood experiences and perceived stress (N = 6780).

female adolescents than in males. Previous research suggested that this has to do with women taking on more responsibility for things such as housework and caring for peers.⁴⁶ In our study, the incidence of bruxism in senior high school students was significantly higher than that in junior high school students, which may be related to the higher levels of aggression, anxiety, depression they experience, as well as greater academic pressure faced by senior high

Table 2 Logistic Regression Analyses with Bruxism as Dependent Variables (N = 6780)

Variables	B	SE	OR	95% CI	P	Cohen's d
Gender						
Male	-	-	1			
Female	0.07	0.06	1.08	0.96–1.21	0.215	0.044
Grade						
Junior high school			1			
Senior high school	0.27	0.06	1.31	1.15–1.48	<0.001	0.149

(Continued)

Table 2 (Continued).

Variables	B	SE	OR	95% CI	P	Cohen's d
Left behind children						
No	–	–	1			
Yes	0.14	0.08	1.15	1.00–1.32	0.056	0.077
Exam results						
Bad	–	–	1			
Moderate	–0.16	0.07	0.86	0.75–0.98	0.022	0.083
Good	–0.31	0.08	0.74	0.63–0.86	<0.001	0.165
Childhood maltreatment	0.27	0.02	1.31	1.26–1.38	<0.001	0.149
Household dysfunction	0.28	0.03	1.32	1.24–1.41	<0.001	0.154
Other adversity	0.51	0.05	1.67	1.51–1.84	<0.001	0.281
ACEQ-R total score	0.16	0.01	1.18	1.15–1.21	<0.001	0.094
Total perceived stress	0.08	0.01	1.08	1.07–1.09	<0.001	0.044
Subjects' perception of stress	0.10	0.01	1.10	1.09–1.12	<0.001	0.052
Ability of cope with stress	–0.01	0.01	0.99	0.98–1.01	0.229	–0.010

Abbreviations: SE, standard error; CI, confidence interval; OR, odds ratio.

school students compared to junior high school students, which are risk factors for bruxism.⁴⁷ Our study also found that the lower the academic performance, the higher the incidence of bruxism. In traditional Chinese culture, In Chinese tradition, all things are inferior except study. Therefore, Chinese parents pay too much attention to their children's academic performance. As a result, the worse the academic performance of teenagers, the greater the pressure, and the higher the incidence of psychological problems and sleep disorders.^{48–50}

Our study found that, compared to adolescents without bruxism, adolescents with bruxism experienced more severe childhood adversity, including childhood maltreatment, household dysfunction, and other adversities, which are risk

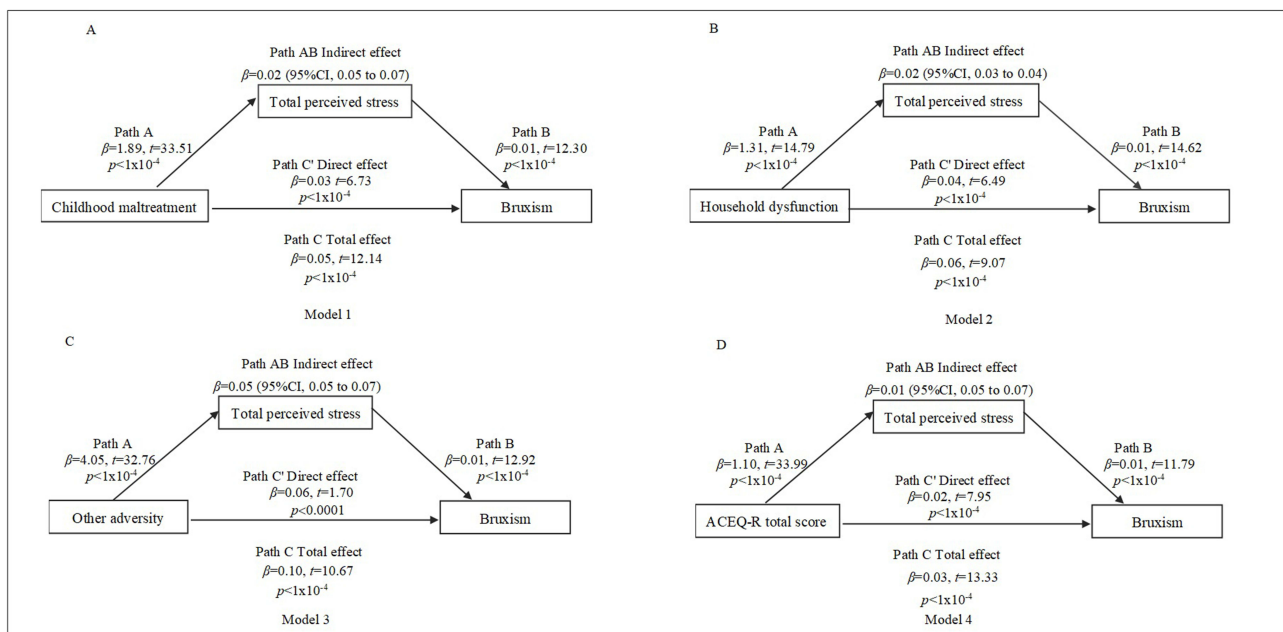


Figure 3 (A) shows Model 1 Path diagram of the mediation model (X=Childhood maltreatment; Y=Bruxism; total perceived stress as mediators). Path C and Path C' represents the total and direct effect between childhood maltreatment and bruxism. (B) Shows Model 2 Path diagram of the mediation model (X=Household dysfunction; Y=Bruxism; total perceived stress as mediators). Path C and Path C' represents the direct effect between household dysfunction and bruxism. (C) Shows Model 3 Path diagram of the mediation model (X=Other adversity; Y=bruxism; total perceived stress as mediators). Path C and Path C' represents the total and direct effect between other adversity and bruxism. (D) Shows Model 4 Path diagram of the mediation model (X=AC; Y=bruxism; total perceived stress as mediators). Path C and Path C' represents the total and direct effect between other adversity and bruxism. Path AB represents the mediation effect and is significant at $p<0.05$ in all the models.

factors for bruxism. Childhood adversity causes adolescents to suffer chronic stress, pain, and adaptive load for a long time which activates the hypothalamic-pituitary-adrenal (HPA) axis and increases the secretion of salivary cortisol; this leads to the instability, degeneration, and attenuation of key neural pathways such as dopamine in the cerebral cortex, which are closely related to the activities of oral and facial involuntary muscles.⁵¹ In addition, childhood adversity causes the amygdala, to over-activate the midbrain nucleus and the motor trigeminal nucleus, leading to rhythmic jaw muscle activity.⁵² The influence of childhood adversity on bruxism may also be related to changes in central serotonin levels and 5-HT2A receptor genotype, causing secondary bruxism.^{53,54}

Our study found that, compared with adolescents without bruxism, adolescents with bruxism had a higher perception of stress and total perceived stress, which were risk factors for bruxism. Perceived stress, which primarily assesses the degree to which an individual feels unpredictable, uncontrollable, or overburdened in their life, has been shown to affect bruxism in previous studies.^{19,55} According to Freud's psychoanalytic theory, the mouth expresses tension; hence, the grinding movement may be a way to disperse emotional tension.⁵⁶ Studies have found that pressure can be relieved after masticatory muscle rhythmic movement (RMMA), and bruxism may be an emergency exit when mental overload occurs.^{18,57}

Our study found that perceived stress mediates the relationship between childhood trauma and bruxism. There is a close relationship between childhood trauma and perceived stress. According to the stress sensitization or effect modification hypothesis, individuals with childhood trauma respond more acutely to stressors and perceive higher levels of stress, which increase according to the number of adverse childhood experiences.^{31,58} Many studies have confirmed that childhood trauma can mediate the occurrence of mental disorders, such as anxiety, depression, suicidal ideation, and perceived stress in adolescents.³⁴ However, our study is the first to demonstrate that childhood trauma mediates bruxism through perceived stress.

Our study has some limitations. First, this is a cross-sectional study, which limits the inference of causality to a certain extent. Although the childhood trauma had occurred previously, the mediation effect model can indicate a certain direction when discussing the influence of independent variables on dependent variables; however, it cannot fully draw inferences about causality. Second, this study used a scale assessment and lacked objective assessment indicators and methods. Third, the mechanism of bruxism caused by childhood trauma through perceived pressure is unclear and may involve neurobiology and imaging, such as changes in the HPA axis, cortisol, amygdala, and other structures, which warrant further study. Therefore, prospective cohort studies, combined with biological indicators, and longitudinal follow-up observations are needed to further explore the mechanisms of bruxism caused by childhood trauma.

Conclusions

Our study found that there is a high incidence of bruxism among Chinese adolescents, and childhood trauma has a significant impact on bruxism. Therefore, childhood trauma should be assessed when diagnosing bruxism. Perceived stress increases the risk of bruxism and is a mediator between childhood trauma and bruxism. Therefore, attention should be paid to the influence of psychological factors on the occurrence of bruxism, and psychological intervention should be involved in the treatment of bruxism.

Data Sharing and Declaration

The datasets generated and/or analyzed during the current study are not publicly available but are available from the corresponding author upon reasonable request.

Ethics Approval and Informed Consent

Formal approval for the study was obtained from the Ethics Committees of Beijing HuiLongGuan Hospital. All participants and their guardians provided written informed consent to indicate their willingness to participate. The study was conducted in accordance with the Helsinki Declaration of 1975, as revised in 2008.

Acknowledgments

The authors would like to thank all the subjects who participated in this study. We would like to thank Editage (www.editage.cn) for English language editing.

Author Contributions

LLW: formal analysis, methodology, writing original draft; SJZ and MQ: data curation, investigation, writing original draft; HJL, JZ and JLL: conceptualization, investigation, writing original draft, resources, YLT and JXC: conceptualization, data curation, writing – review & editing. All authors gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

Funding

This research was supported by the National Key Research and Development Program of China (2021YFC2501504); Beijing Huilongguan Hospital Longyue Plan Fund Project (LY202402); Beijing Municipal Administration of Hospitals Incubating Program (PX2025066).

Disclosure

The authors declare that there are no possible conflicts of interest for this study.

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