

# The Effect of Peer Relationships on Adolescent Loneliness: The Role of Psychological Resilience and the OXTR Gene

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**Background:** Based on the gene-environment interaction paradigm, this study explored the effect of peer relationships on adolescent loneliness and the role of psychological resilience and the oxytocin receptor gene (OXTR).

**Methods:** A survey was conducted in a sample of 619 adolescents, and their oral cells were collected for DNA extraction and genotyping.

**Results:** The results showed that (1) both peer relationships and psychological resilience significantly affected adolescent loneliness; (2) psychological resilience partially mediated the relationship between peer relationships and loneliness in adolescents; (3) OXTR gene rs53576 polymorphism moderated both the first and second half of the indirect pathway of the mediation model. Specifically, carriers of the rs53576 polymorphism A/A genotype showed a significantly enhanced effect of peer relationships on adolescent psychological resilience, while carriers of the rs53576 polymorphism G/G genotype showed a significantly enhanced effect of psychological resilience on adolescent loneliness.

**Conclusion:** These findings helped elucidate the developmental mechanisms of adolescent loneliness in terms of peer relationships, psychological resilience, and OXTR gene polymorphisms.

**Plain Language Summary:** A moderated mediation effects analysis was conducted to investigate the effect of peer relationships on adolescent loneliness and the role of psychological resilience and the oxytocin receptor gene (OXTR). The results revealed psychological resilience partially mediated the relationship between peer relationships and loneliness in adolescents; OXTR gene rs53576 polymorphism moderated both the first and second half of the indirect pathway of the mediation model. These findings helped elucidate the developmental mechanisms of adolescent loneliness in terms of peer relationships, psychological resilience, and OXTR gene polymorphisms.

**Keywords:** peer relationship, adolescents, loneliness, psychological resilience, OXTR gene

## Introduction

Baumeister and Leary (1995) have proposed that humans are born with an innate need to connect with others, and that when this need is unfulfilled, they will experience loneliness.<sup>1</sup> Loneliness is described as a negative and distressing emotional state resulting from the discrepancy between an individual's desired social connection and their actual social connection.<sup>2</sup> As a negative psychological state, loneliness is closely linked to an individual's mental health.<sup>3,4</sup> Adolescence is identified as a critical period for individuals as they transition from childhood to maturity, and it is also recognized as a peak period for loneliness.<sup>5,6</sup> At this stage, adolescents' autonomy is gradually increasing, and their social connections are beginning to shift from family to peers. Faced with the developmental challenges of adolescence and a changing social environment, adolescents may experience an increased sense of separation. During this sensitive period, adolescents are more likely to feel lonely if their needs of belonging are unmet.<sup>5</sup> A recent systematic review

examining the prevalence of loneliness across 113 countries reveals that the pooled prevalence of loneliness among adolescents ranges from 9.2% to 14.4%.<sup>7</sup> Loneliness could significantly impact the psychological well-being of adolescents,<sup>3,4</sup> increasing their susceptibility to insomnia, depression, and suicidal tendencies. Additionally, it could also have affected their social functioning, potentially leading to school dropout and social anxiety. Thus, it is crucial to investigate the developmental mechanisms of adolescent loneliness and its influencing factors to promote the mental well-being of adolescents.<sup>8</sup> Furthermore, the evolutionary theory of loneliness posits that loneliness has a strong genetic basis.<sup>9</sup> However, current research on loneliness has primarily focused on environmental and behavioral studies, with very little research examining the relationship between genes and the environmental context. Therefore, to enrich the study of the genetic-environmental interaction effects of loneliness, this study adopted a gene-environment interaction paradigm perspective to explore the role of the oxytocin receptor gene (OXTR) rs53576 polymorphism and psychological resilience in the relationship between peer relationships and adolescent loneliness.

## Peer Relationships Influence Adolescent Loneliness

Ecosystem theory has suggested that an individual's development is influenced by interactions between the individual themselves and their environment.<sup>10</sup> As a microsystem, the school environment holds the second greatest influence on adolescents, following the family. Within the school ecosystem, peer relationships wield a significant impact on both adolescents' mental health and school adjustment.<sup>11</sup> Adolescence marks a period during which individuals attain more autonomy and individualization. During this stage, peer relationships start to surpass parent-child relationships, gradually becoming adolescents' primary social connections.<sup>12</sup> Self-determination theory posits that interpersonal support, trusted peer relationships, and a sense of belonging are crucial experiences for fulfilling one's basic psychological need for relationships.<sup>13</sup> When an individual's need for relationships goes unfulfilled, the associated distress from this unmet need can lead to the development of loneliness and social-emotional problems.<sup>13–16</sup> Peer relationship issues have been identified as the most direct stressor impeding adolescents' need for relationships, thereby precipitating feelings of loneliness and social-emotional difficulties.<sup>17–19</sup> Peer bullying, rejection, and conflict are among the most common peer relationship problems experienced by adolescents and serve as sources of peer stress, impacting adolescent loneliness, depression, and suicide.<sup>20–23</sup> Concurrently, research indicates that social isolation, school suspensions, and other prevention and control measures—many of which were experienced by adolescents during the COVID-19 pandemic—significantly heighten adolescents' overall feelings of isolation.<sup>24,25</sup> These circumstances, to some extent, curtail adolescents' socialization with their peers, exerting a profound impact on their mental health.<sup>26</sup> In consideration of these findings, the present study proposes:

Hypothesis 1: Peer relationships influence adolescents' loneliness.

## The Mediating Role of Psychological Resilience

Psychological resilience plays a crucial role as a protective factor for individuals confronting adversity<sup>27</sup> and may serve as a mediator between adolescent peer relationships and loneliness. Resilience framework theory posits that the environment in which an adolescent individual resides directly shapes the establishment and enhancement of their psychological resilience.<sup>28</sup> Family and social support systems represent the principal environmental factors influencing adolescents' psychological resilience.<sup>29</sup> Research indicates that close peer relationships contribute to the enhancement of adolescent psychological resilience,<sup>28</sup> while negative peer interactions, such as bullying and rejection, can impede the development of adolescent psychological resilience.<sup>30</sup> Kobak and Sceery (1988) also discovered that groups who felt the need for safety and belonging exhibited higher levels of mental resilience and reported less loneliness, whereas groups who felt rejected had lower mental resilience scores and reported higher levels of loneliness.<sup>31</sup> Psychological resilience has been identified as a crucial protective factor in mitigating adolescent loneliness. Labrague et al (2021) demonstrated that high psychological resilience serves as a protective factor against loneliness.<sup>32</sup> Similarly, in their study on adolescent cyberbullying, psychological resilience, and loneliness, Han et al (2021) showed that psychological resilience significantly reduces adolescent loneliness and acts as a mediator between cyberbullying and adolescent loneliness.<sup>30</sup> Based on these findings, the current study proposes:

Hypothesis 2: Psychological resilience may mediate between peer relationships and adolescent loneliness.

The development of loneliness and psychological resilience in adolescents is not only influenced by the peer environment but also strongly affected by genetics. Existing studies have consistently shown that the OXTR gene is an important candidate gene for loneliness and psychological resilience.<sup>33,34</sup> This gene is located on human chromosome 3p25-3p26.2 and spans 17 kb, with three introns and four exons.<sup>35</sup> OXTR gene receptors are distributed throughout the brain, including in the amygdala, vomeronasal nucleus, ventral medial hypothalamus, and brainstem,<sup>36</sup> and are recognized as playing key roles in resilience and various types of social behavior.<sup>37-39</sup> This gene can moderate individuals' social behaviors such as cognition and social interaction,<sup>40</sup> as well as enhance individuals' psychological resilience by reducing physiological stress responses and promoting social bonding.<sup>40,41</sup> Rs53576, a single nucleotide polymorphism in the third intron of OXTR, has been strongly associated with individual loneliness<sup>42</sup> and psychological resilience.<sup>43</sup> There are two allelic variants of the gene: the A allele (ie, the minor allele) and the G allele (ie, the major allele).<sup>39</sup> Existing studies have shown that individuals carrying one or more G alleles of the OXTR gene rs53576 exhibit stronger adaptive social functioning, whereas those with one or more A alleles exhibit lower adaptive social functioning.<sup>42,44</sup> Krueger et al's research has suggested that individuals with the OXTR gene rs53576 GG genotype exhibit greater prosocial behavior and trust toward others.<sup>45</sup> Additionally, Verhagen et al's study indicates a correlation between the OXTR gene rs53576 genotype and the development of adolescent loneliness.<sup>46</sup> At the same time, a study by Ryan and Ryznar (2022) also suggests that dysregulation of the rs53576 polymorphism of the OXTR gene may be associated with lower levels of psychological resilience, and vice versa.<sup>47</sup> Additionally, Chang et al's study indicates that carriers with specific OXTR rs53576 genotypes might demonstrate greater biological sensitivity and stress reactivity in environmental adaptation.<sup>48</sup> Furthermore, the social salience hypothesis also indicates that oxytocin could increase individuals' sensitivity and responsiveness to social environments.<sup>37</sup> Thus, it could be inferred that the polymorphism of the OXTR gene rs53576 plays an important role in the development of adolescent loneliness and psychological resilience.

## The Moderating Role of the rs53576 Polymorphism of the OXTR Gene

Both the differential susceptibility model and the diathesis-stress model emphasize the influence of gene-environment interactions on individuals. That is, the mechanisms of loneliness and psychological resilience in adolescents are influenced by the interaction of genes and the environment. Moreover, current research also provides an empirical basis for the effects of gene-environment interactions on adolescents' loneliness and psychological resilience. For example, Cicchetti and Rogosch (2012) found that the magnitude of the difference in psychological resilience between maltreated children carrying the OXTR gene rs53576 AA or AG genotype and non-maltreated children was greater than that of children with the GG genotype.<sup>49</sup> Bradley et al (2013) showed that individuals carrying the OXTR gene rs53576 GG and AG genotypes had higher levels of positive affect and psychological resilience in positive environments.<sup>50</sup> Likewise, Olf (2012) found that the OXTR gene could increase individuals' psychological resilience by reducing physiological stress responses and promoting social connectedness.<sup>41</sup> Peer relationships are particularly important for adolescents and have a strong impact on their psychological resilience.<sup>28,30</sup> It has been suggested that the rs53576 polymorphism of the OXTR gene may moderate the effect of peer relationships on adolescents' psychological resilience. Therefore, this study proposes:

Hypothesis 3: The rs53576 polymorphism of the OXTR gene may moderate the relationship between peer relationships and psychological resilience in adolescents.

Furthermore, it has been shown that adolescents with the A allele of the rs53576 polymorphism of the OXTR gene have higher levels of loneliness in negative environments.<sup>23</sup> The rs53576 polymorphism of the OXTR gene is understood to play an important role in the social and emotional functioning of individuals during interactions with environmental risks or stressors.<sup>51</sup> Psychological resilience is a protective factor in the face of environmental risks or stressors and has a significant impact on adolescents' feelings of isolation.<sup>32</sup> Meanwhile, Kohlhoff et al (2022) have indicated that the rs53576 polymorphism of the OXTR gene may moderate the effects of social support or other protective factors or

resilience mechanisms on adolescents' social, emotional, and behavioral functioning.<sup>51</sup> This suggests that the rs53576 polymorphism of the OXTR gene may moderate the effects of psychological resilience on adolescent loneliness. With this in mind, the current study proposed:

Hypothesis 4: The rs53576 polymorphism of the OXTR gene may moderate the relationship between psychological resilience and loneliness in adolescents.

In summary, this study aimed to construct a moderated mediation model to explore the mediating effect of psychological resilience between peer relationships and adolescent loneliness, as well as the moderating role of the rs53576 polymorphism of the OXTR gene in this mediating effect. The goal is to provide empirical evidence to enrich current and future research on adolescent loneliness from the gene-environment interaction paradigm.

## Methodology

### Participants

The participants in this study were selected from a junior school in Hunan Province. Questionnaires and genetic samples were collected using a cluster sampling method (with the class as the unit for the survey). It is worth noting that effect sizes for conducting gene-environment interaction studies typically range from 0.01 to 0.02.<sup>52</sup> Sample size estimation was conducted using G\*Power 3.1.9.3 software, indicating that a minimum of 395 to 787 subjects would be required to achieve more than 80% statistical power. Therefore, a total of 785 students were surveyed in this study. After excluding invalid samples (eg, due to careless or incomplete responses, reports of a history of mental illness, and refusal to participate in the survey), 619 valid subjects remained, resulting in a valid response rate of 79% for the questionnaire, meeting the statistical test requirement for sample size. Among them, 326 (52.7%) were male students and 293 (47.3%) were female students. The average age of participants was  $13.93 \pm 0.40$ .

### Procedure

Participants were selected from a junior school in Hunan Province and surveyed using a cluster sampling method. First, the study was approved by the Ethics Committee of Hunan Normal University. Second, informed consent was obtained from the school, teachers, parents, and student participants. Finally, paper questionnaires and genetic samples were collected from the subjects during mental health education classes. The experimenters consisted of MSc and PhD students with a background in psychology, with no fewer than 10 experimenters per test. Before commencing the formal collection of genetic samples, professional genetic sample collectors trained the MSc and PhD students to collect the genetic samples in this study. After receiving training, the PhD students and MSc students practiced sampling each other in pairs to ensure familiarity with the collection technique. Meanwhile, before collecting genetic samples, student subjects were informed in advance that mouth swab genetic sampling would be required as part of the study. During the formal testing process, subjects first completed the questionnaire (which took about 10–20 minutes) and then proceeded to the corresponding gene sampling group for sampling, according to their assigned numbers. After completing both the survey and genetic sampling, each subject received a small gift as a reward, such as pens, notebooks, and other school supplies needed daily by students.

### Collection of Genetic Samples, Extraction, and Genotyping

In this study, genetic samples from the study subjects were collected using oral swabs. To ensure sample quality and prevent contingencies, two oral swab samples were collected from each subject. Each collected oral swab was packaged, and once all the day's samples were collected, they were immediately sent to the company in a sample box by a technician from the professional company. After all the oral swabs were collected, DNA was extracted and purified using a genomic DNA extraction kit. Genotyping was performed using the imLDR typing technique for the rs53576 polymorphism of the OXTR gene.

## Measurements

### Loneliness

Loneliness was measured using the 12-item peer-related subscale of the Louvain Loneliness Scale for Children and Adolescents (LLCA).<sup>53</sup> The scale was translated into Chinese using the back-translation method by two English PhDs and was evaluated by a panel of 10 experts consisting of psychology professors, PhDs, and frontline psychology teachers. The scale comprises 12 items (eg, “I feel lonely at school”) rated on a 4-point scale ranging from 1 (never) to 4 (often). The total score on the scale ranges from 12 to 48, with higher scores indicating higher levels of loneliness among adolescents compared to their peers. The Cronbach’s  $\alpha$  coefficient for the items was 0.91 in this study.

### Psychological Resilience

Psychological resilience was measured using the Resilience Scale developed by Connor and Davidson (2003).<sup>54</sup> It was revised by Ye et al (2016) and is now widely used in China.<sup>55</sup> It contains 10 items (eg, “When things change, I can adapt”), each one scored on a scale ranging from 0 (never) to 5 (almost always) points, resulting in a total possible score of 0 to 50 points. The higher the total score, the higher the respondent’s psychological resilience. The Cronbach’s  $\alpha$  coefficient for the items was 0.99 in this study.

### Peer Relationships

Peer relationships were measured using the Friendship Quality Questionnaire as developed by Parker and Asher (1993),<sup>56</sup> which was revised by Zhou et al (2006) and has since become widely used in China.<sup>57</sup> It contains 18 items (eg, “This friend and I make each other feel important and special”), each scored on a scale ranging from 1 (completely inconsistent) to 5 (completely consistent) points, with a total possible score range of 18 to 90 points. Higher total scores indicate that the respondent has better peer relationships. The Cronbach’s  $\alpha$  coefficient for the items was 0.90 in this study.

## Data Processing and Analysis Method

The data were entered into Excel in a double-blind manner, and simultaneously, the validity of the data was established based on the value range of each scale during entry to avoid inputting incorrect or abnormal values. Finally, SPSS was utilized for data cleaning, transformation, and analysis. Data analysis was conducted using SPSS 26.0 and the SPSS macro program PROCESS. First, the Hardy-Weinberg equilibrium test was performed to assess the distribution of genes. Second, analysis of variance was employed to detect differences in the OXTR gene rs53576 polymorphism in peer relationships, psychological resilience, and loneliness, while correlation analysis was used to identify the relationships among peer relationships, psychological resilience, and loneliness. Finally, a moderated mediation effects analysis was conducted using the SPSS macro program PROCESS MODEL58 to examine the effect of peer relationships on adolescent loneliness and the roles of psychological resilience and the oxytocin receptor gene (OXTR). The bias-corrected 95% confidence interval (CI) was calculated with 5000 bootstrapping re-samples. If the 95% CI did not contain 0, it indicated that the effect was significant, and the conditional effects were plotted. All statistical analyses were performed using SPSS 26.0. Statistical significance was defined as a two-tailed value of  $< 0.05$ . Additionally, all models were controlled for covariates (gender), and the study variables were standardized.

## Results

### Data Availability Test

As the data in this study were obtained through students’ self-reporting, common method bias may occur. Therefore, an exploratory factor analysis was conducted using Harman’s one-way test for all items of each of the three scales. The Results showed that 6-factor eigenvalues were  $> 1$ , and the variance explained by the first factor was 26% ( $< 40\%$ ). This indicates that the data were not significantly influenced by common method bias.

The genotype distribution of the OXTR locus was as follows: rs53576: A/A = 280 (45.2%), G/A = 275 (44.4%), and G/G = 64 (10.3%). The Hardy-Weinberg equilibrium test showed that the observed values at the loci were well-aligned with the expected values (rs53576:  $\chi^2 = 0.09$ ,  $p > 0.05$ ). Additionally, the Minor Allele Frequency (MAF) in this study was rs53576: 0.651  $> 0.05$ .

## Analysis of Variance of OXTR Gene rs53576 Polymorphism in Peer Relationships, Psychological Resilience, and Loneliness

The results of the ANOVA are shown in Table 1. The rs53576 polymorphism of the OXTR gene did not differ significantly in peer relationships, psychological resilience, or loneliness, suggesting that genes and environmental factors were independent of one another. Therefore, the effect of genes associated with environmental factors on the results could be excluded, in line with the gene-environment interaction research paradigm.<sup>58</sup>

## Descriptive Statistics and Correlation Analysis

The results of the correlation analysis are shown in Table 2. Peer relationships positively correlated with adolescent psychological resilience. Significant negative correlations were found between peer relationships, psychological resilience, and adolescent loneliness.

## The Effect of Peer Relationships on Adolescent Loneliness: A Moderating Mediation Test

A moderated mediated effect analysis was performed using PROCESS macro 3.0 in SPSS. Before beginning the statistical analysis, all continuous variables were standardized, and gender was included as a control variable. The results are shown in Table 3. In Equation 1, gender, peer relationships, and psychological resilience all significantly predicted adolescent loneliness ( $\beta_{\text{gender}} = 0.25, p < 0.01$ ;  $\beta_{\text{Peer Relationships}} = -0.30, p < 0.001$ ;  $\beta_{\text{Psychological Resilience}} = -0.26, p < 0.001$ ). In Equation 2, gender, peer relationships, and the interaction term between peer relationships and the OXTR gene rs53576 all significantly predicted adolescent psychological resilience ( $\beta_{\text{gender}} = -0.36, p < 0.001$ ;  $\beta_{\text{Peer Relationships}} = 0.55, p < 0.001$ ;  $\beta_{\text{XW1}} = -0.22, p = 0.004$ ). This demonstrated that peer relationships, psychological resilience, adolescent loneliness, and the OXTR gene rs53576 were all a part of the moderated mediation model: psychological resilience partially mediated the relationship between adolescent peer relationships and loneliness; rs53576 polymorphism moderated both the first- and second-half pathways of this mediation model, which is to say that rs53576 polymorphism moderated both the effect of peer relationships on adolescent psychological resilience and the effect of psychological resilience on adolescent loneliness. Table 4 presents the mediation effect values for psychological resilience across genotypes.

**Table 1** Analysis of Variance of OXTR Gene rs53576 Polymorphism in Peer Relationships, Psychological Resilience, and Loneliness

Variables	A/A	G/A	G/G
Loneliness	21.13±7.73	21.16±7.60	20.75±7.98
Peer relationships	66.92±12.26	68.69±12.64	68.55±12.79
Psychological resilience	27.62±8.70	28.82±7.84	29.19±8.33
F	0.08	1.50	1.86
p	0.93	0.22	0.16

**Table 2** Descriptive Statistics and Correlation Analysis Between Peer Relationships, Psychological Resilience, and Loneliness

Variables	Peer Relationship	Psychological Resilience	Loneliness
Peer relationship	I		
Psychological resilience	0.41**	I	
Loneliness	-0.40**	-0.40**	I
M ± SD	67.88 ± 12.50	28.31 ± 8.30	21.11 ± 7.69

Note: \*\*p < 0.01.

**Table 3** The Effect of Peer Relationships on Adolescent Loneliness: The Mediation of Psychological Resilience and the Moderation of rs53576 Polymorphism in the OXTR Gene

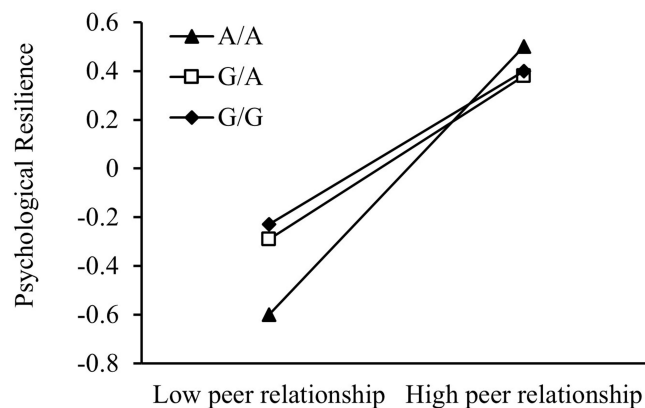
Variables	Model 1 (Dependent Variable: Loneliness)				Model 2 (Dependent Variable: Psychological Resilience)				Model 2 (Dependent Variable: Loneliness)			
	$\beta$	t	p	95% CI	$\beta$	t	p	95% CI	$\beta$	t	p	95% CI
Gender	0.25	<b>3.40**</b>	<b>&lt; 0.01</b>	[0.10,0.39]	-0.36	<b>4.91***</b>	<b>&lt;0.001</b>	[-0.50,-0.21]	0.25	<b>3.48***</b>	<b>&lt; 0.01</b>	[0.11, 0.39]
X	-0.30	<b>-7.72***</b>	<b>&lt; 0.001</b>	[-0.38, -0.23]	0.55	<b>10.07***</b>	<b>&lt; 0.001</b>	[0.44, 0.66]	-0.31	<b>-7.89***</b>	<b>&lt; 0.001</b>	[-0.39,-0.23]
W1					0.10	1.26	0.21	[-0.05, 0.24]	0.08	1.01	0.31	[-0.07, 0.22]
W2					0.14	1.09	0.28	[-0.11, 0.38]	0.08	0.66	0.51	[-0.16, 0.32]
XW1					-0.22	<b>-2.86</b>	<b>0.004</b>	[-0.37, -0.07]				
XW2					-0.23	-1.90	0.06	[-0.47, 0.01]				
M	-0.26	<b>-6.56***</b>	<b>&lt; 0.001</b>	[-0.34,-0.18]					-0.21	<b>-3.93***</b>	<b>&lt; 0.001</b>	[-0.32,-0.11]
M*W1									-0.04	-0.57	0.57	[-0.19, 0.10]
M*W2									-0.29	<b>-2.35*</b>	<b>0.019</b>	[-0.52, -0.05]
R <sup>2</sup>	0.24				0.21				0.25			
F	<b>63.777***</b>				<b>27.56***</b>				<b>28.41***</b>			

**Notes:** X = peer relationships; W1 = GA vs AA; W2 = GG vs AA; XW1 is the interaction term between peer relationships and rs53576 being virtualized as W1; XW2 is the interaction term between peer relationships and rs53576 being virtualized as W2; M = psychological resilience; M\*W1 is the interaction term between psychological resilience and rs53576 being virtualized as W1; M\*W2 is the interaction term between psychological resilience and rs53576 being virtualized as W2; bolded font indicates the value is significant, \* $p < 0.05$ , \*\* $p < 0.01$ , \*\*\* $p < 0.001$ .

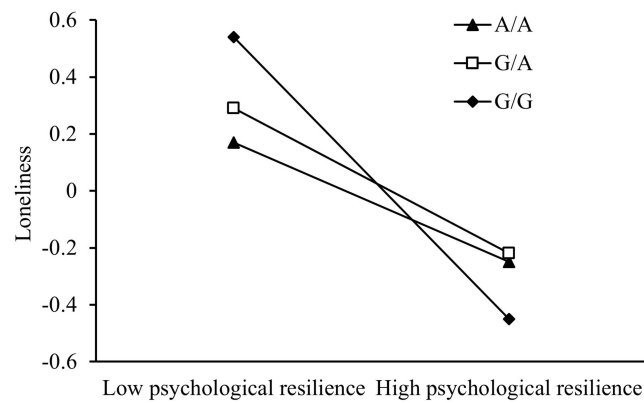
**Table 4** The Mediating Effects of Psychological Resilience on Different Genotypes

Independent Variable	rs53576 Genotypes	Mediating Effect	Bootstrap SE	95% CI
Peer relationship	A/A	-0.12	0.03	[-0.19, -0.05]
	G/A	-0.08	0.02	[-0.13, -0.04]
	G/G	-0.16	0.07	[-0.29, -0.04]

To further explain the moderating effect, a simple slope test was conducted to examine the moderating effect of rs53576 (see Figures 1 and 2). Specifically, peer relationships positively predicted adolescent psychological resilience when individuals carried the rs53576 polymorphism G/A and G/G genotypes:  $\beta = 0.33$ ,  $t = 6.22$ ,  $m < 0.001$ ; and  $\beta = 0.32$ ,  $t = 2.87$ ,  $p < 0.01$ , respectively. However, when individuals carried the rs53576 polymorphism A/A genotype, the prediction of adolescent psychological resilience by peer relationships was significantly enhanced, as evidenced by an increased slope:  $\beta = 0.55$ ,  $t = 10.07$ ,  $p < 0.001$ . When individuals carried the rs53576 polymorphisms A/A and G/A genotypes, psychological resilience negatively predicted adolescent loneliness: ( $\beta = -0.21$ ,  $t = -3.93$ ,  $p < 0.001$ ; and



**Figure 1** The simple slope plot between peer relationships and psychological resilience.



**Figure 2** The simple plot between psychological resilience and loneliness.

$\beta = -0.25$ ,  $t = -4.38$ ,  $p < 0.001$ , respectively. However, when individuals carried the rs53576 polymorphic G/G genotype, the negative prediction of psychological resilience on adolescent loneliness was significantly enhanced, with an increased slope:  $\beta = -0.50$ ,  $t = -4.48$ ,  $p < 0.001$ .

## Discussion

The developmental mechanisms of loneliness are influenced by a combination of genetic, psychological, and social environmental factors. In this study, we explored the mechanism of the role of the OXTR gene rs53576 polymorphism and psychological resilience in the relationship between peer relationships and adolescent loneliness by constructing a moderated mediation model from a gene-environment interaction paradigm. The results suggest that peer relationships can affect adolescents' loneliness not only directly but also through the mediating effect of psychological resilience. Meanwhile, OXTR gene rs53576 polymorphism was seen to moderate both the first and second half of this mediating pathway, in that OXTR gene rs53576 polymorphism could not only moderate the effect of peer relationships on adolescent psychological resilience but also the effect of psychological resilience on adolescent loneliness. The results validated the research hypotheses, providing an empirical basis for enriching research on the genetic and environmental interaction effects of adolescent loneliness, as well as providing theoretical support for the development of scientific prevention and intervention tactics on adolescent loneliness.

The results of the correlation and regression analysis show that peer relationships are negatively correlated with adolescents' loneliness and negatively predict adolescents' loneliness, which is consistent with the findings of other existing studies.<sup>59,60</sup> That is, close peer relationships can help adolescents feel less isolated; however, bullying, conflict, or rejection in peer relationships can increase adolescents' feelings of isolation. Adolescence is a peak period of loneliness for many as they navigate a "psychological weaning period".<sup>61</sup> Adolescents are beginning to break away psychologically from their parents' protection and diminishing their attachment to their parents as they gradually develop into independent individuals. Meanwhile, peer relationships are gradually surpassing parent-child relationships, becoming the most important interpersonal relationships for adolescents. During this sensitive period, sudden shifts can cause adolescents to experience anxiety and internal conflict, as well as incite increased feelings of separation. When their practical needs for social connection are not met, adolescents become particularly vulnerable to loneliness.<sup>5</sup> At the same time, self-determination theory states that interpersonal support, trusted peer relationships, and a sense of belonging are fundamental experiences that satisfy individuals' basic psychological needs for relationships.<sup>13</sup> When individuals' relationship needs are unmet, the associated distress can drive individuals to experience loneliness and social-emotional problems.<sup>13-16</sup> Thus, peer relationships are an important influence on adolescents' feelings of loneliness, and helping adolescents form close peer relationships is crucial to promoting the positive development of adolescents' mental health.



This study also found that peer relationships can impact adolescents' loneliness through the mediating effect of psychological resilience, a phenomenon confirmed in other existing studies. For example, a study on the effects of psychological resilience, peer relationships, and teacher-student relationships on students' mental health issues during the Covid-19 pandemic demonstrated that peer aggression was associated with greater mental health issues in students, and that psychological resilience is a contributing factor to improving students' mental health while also buffering the negative impact of peer aggression on students' mental health.<sup>62</sup> Meanwhile, another study on cyberbullying, psychological resilience, and loneliness during the pandemic among rural Chinese adolescents showed that psychological resilience significantly reduced loneliness among rural adolescents and buffered the effect of cyberbullying on adolescent loneliness.<sup>30</sup> This suggests that psychological resilience, as an important protective factor for individuals under stress, is not only influenced by the individual's environment<sup>28</sup> but also plays an important role in affecting the individual's mental health.<sup>32</sup> In other words, positive environments such as close peer relationships and a high level of social support can enhance adolescents' psychological resilience and help improve their mental health, thereby reducing the generation of negative emotions such as loneliness. Nevertheless, negative environments such as bullying, rejecting, or aggressive peer relationships, and low social support can reduce adolescents' psychological resilience and have a negative impact on adolescents' mental health, increasing the occurrence of negative emotions. It is thus clear that enhancing the psychological resilience of adolescents is critical to helping improve their mental health.

The results of the moderated mediation analysis showed that the rs53576 polymorphism of the OXTR gene moderated both the first and second halves of the mediating pathway from peer relationships to psychological resilience, affecting adolescent loneliness. OXTR gene rs53576 polymorphism moderated not only the effect of peer relationships on adolescent psychological resilience but also the effect of psychological resilience on adolescent loneliness. Specifically, the effect of peer relationships on adolescent psychological resilience was significantly enhanced in OXTR gene rs53576 polymorphism A/A genotype carriers, showing an increased slope. Meanwhile, the effect of psychological resilience on adolescent loneliness was significantly enhanced in OXTR gene rs53576 polymorphism G/G genotype carriers, also showing an increased slope. This result was supported by the social salience hypothesis. Specifically, carriers of the A/A and G/G genotypes exhibited heightened sensitivity to environmental cues, making them more susceptible to the influence of their environment, thus displaying higher or lower levels of psychological resilience and loneliness.<sup>37</sup>

The results of this study suggested that adolescents with the A/A genotype exhibited higher environmental sensitivity compared to those with the G/G or G/A genotypes, particularly regarding peer relationships and psychological resilience. Existing research indicated that individuals with the A/A genotype were more influenced by their environment; that is, those carrying the A/A genotype tended to experience more negative outcomes when exposed to more negative environments, such as lower positive affect,<sup>44</sup> lower empathy,<sup>63</sup> and lower self-esteem,<sup>64</sup> whereas they experienced more positive outcomes when exposed to more positive environments. This could be attributed to the A/A genotype's association with morphological changes in the hypothalamus and amygdala, as well as greater stress responsiveness.<sup>65</sup> Compared to the G/G genotype, carriers of the A/A genotype had smaller hypothalamic volumes, leading to increased coupling between the hypothalamus and the amygdala and dorsomedial prefrontal cortex during facial emotion processing or stress-related tasks, resulting in structural and functional alterations in the individual's limbic-hypothalamic circuitry and heightened sensitivity to stressors and emotional responses.<sup>66</sup> Therefore, individuals with the A/A genotype were more likely to pay attention to stress-related environmental cues and demonstrate higher sensitivity to stress-related factors such as peer relationships.

However, in terms of psychological resilience and loneliness, adolescents with the G/G genotype exhibited higher environmental sensitivity compared to those with the A/A or G/A genotypes. Existing research suggested that individuals with the G/G genotype were more influenced by their environment; that is, people carrying the G/G genotype tended to experience more negative outcomes when exposed to more negative environments,<sup>67</sup> higher emotional dysregulation and disorganized attachment,<sup>68</sup> whereas they experienced more positive outcomes when exposed to more positive environments. This may have been because individuals with the G/G genotype seemed more receptive to social cues and influenced by positive environments.<sup>66,69</sup> Since individuals with the G/G genotype had higher reward dependency,<sup>66</sup> it increased their sensitivity to positive environments, making them more likely to benefit from social support and psychological resilience,<sup>70</sup> buffering the effects of stress on

individuals.<sup>50</sup> Therefore, carriers of the G/G genotype were more likely to pay attention to positive environmental cues, showing higher sensitivity to positive environmental factors such as psychological resilience. Additionally, different susceptibility models also suggested that risk genes were plastic, and more plastic individuals were more sensitive to both positive and negative environments. Compared to individuals without plasticity genes, individuals with plasticity developed “better” in positive environments but “worse” in negative environments.<sup>71</sup> Therefore, in future research, we needed to shape positive environments (such as positive peer relationships, high psychological resilience, etc). According to individuals’ genetic susceptibility, they could develop better in positive environments, thereby reducing the occurrence of adolescent loneliness. For example, identifying individuals at risk for loneliness and low resilience based on genetic markers early in life allows for targeted interventions to be implemented during critical developmental stages. Early intervention programs focused on promoting social-emotional development and resilience-building skills can help mitigate the negative impact of genetic predispositions on psychological well-being.

Working within the gene-environment interaction paradigm, the current study addressed genetic, psychological, and social factors of loneliness and explored the mechanism of the role of OXTR gene rs53576 polymorphism, psychological resilience in peer relationships, and adolescent loneliness. It enriches our understanding of the gene-environment interaction effect of loneliness and provides an empirical basis for the intervention into and prevention of adolescent loneliness. However, this study still has some shortcomings. First, many genetic, psychological, and social factors influence adolescent loneliness. This study explored only the interaction effects of peer relationships, psychological resilience, and the rs53576 polymorphism of the OXTR gene on adolescent loneliness. Future research could discuss the effects of other psychological and social factors interacting with genes, such as the impacts of dopamine and the HPA axis on adolescent loneliness. Moreover, an increasing number of researchers advocate for considering loneliness as a multidimensional phenomenon,<sup>72,73</sup> Therefore, future research needs to further explore whether there are differences in the influencing factors and mechanisms of loneliness across different dimensions. Second, loneliness has also been shown to be strongly influenced by several different genes. The combined effect of multiple genes, compared to single genes, offers a better explanation of the developmental mechanism of loneliness, and the genetic explanation rate of multiple genes is also greater than that of single genes. Finally, due to limited funding, this study adopted a cross-sectional design, with all participants being students in one grade at the same school. Future studies should expand the sample size as well as examine the gene-environment interaction effects of loneliness from a dynamic longitudinal perspective.

## Conclusion

To conclude, the current study found that: (1) peer relationships and psychological resilience significantly affected adolescent loneliness; (2) psychological resilience partially mediated the relationship between peer relationships and adolescent loneliness; and (3) rs53576 polymorphism of the OXTR gene moderated both the first and second halves of the pathway of the mediation model, as evidenced by the significantly enhanced effect of peer relationships on adolescent psychological resilience in carriers of the rs53576 polymorphism A/A genotype, and the significantly enhanced effect of psychological resilience on adolescent loneliness in carriers of the rs53576 polymorphism G/G genotype.

## Ethics Approval

The survey was conducted under the Declaration of Helsinki as revised in 1989 and approved by the Ethics Committees of Hunan Normal University (2022001). Informed consent was obtained from all individual participants included in the study.

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## Disclosure

The authors report no conflicts of interest in this work.

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