



OXTR rs53576 polymorphism impacts interpersonal adaptability: Dispositional forgiveness as a mediator

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ABSTRACT

Polymorphisms in the oxytocin receptor (*OXTR*) gene have been shown to be related to individual differences in social skills that are important for building and maintaining social relationships, such as the capability to efficiently process social information and regulate emotions. However, what remains unclear is the potential roles of *OXTR* polymorphisms in interpersonal adaptability, namely the ability to cope with the situational demands of interpersonal interactions. In this study, we examined the roles of *OXTR* rs53576 polymorphism in interpersonal adaptability, empathic perception, and dispositional forgiveness in a cohort of 573 college freshmen. The results indicated that the scores on interpersonal adaptability and dispositional forgiveness, apart from empathic perception, increased as functions of the number of G alleles of *OXTR* rs53576. Moreover, dispositional forgiveness, but not empathic perception, mediated the association between *OXTR* rs53576 and interpersonal adaptability. The findings highlight the influences of the *OXTR* gene on adaptive interpersonal interactions, especially when individuals face changing social situations.

1. Introduction

In the fast-changing modern world, the pace and types of change we are experiencing continue to grow, calling for an increasingly high level of adaptability in the workplace and other social contexts. Interpersonal adaptability refers to individuals' psychological characteristics and ability to cope with interpersonal interactions in changing situations. It reflects the fitness of one's interpersonal behaviors, thoughts, and emotions with the situational demands of interpersonal interactions (Chan, 2000; Oliver, 2012). In response to dynamic situational demands, some individuals adapt quickly and fit well in new environments. Others may fail to adjust to the new situations and suffer hardship. It has been shown that individual differences in interpersonal adaptability can predict the outcomes of one's social interactions (Pulakos et al., 2000) and subjective well-being (Zhao, 2012). Although interpersonal adaptability is fundamental to social functioning, the genetic basis of this remarkable trait remains unexplored.

Previous studies have shown that robust genetic predispositions

contribute to interpersonal processes (Klahr et al., 2013; Markey et al., 2015) and social skills (Knafo et al., 2008; Toccaceli et al., 2018). A large body of empirical research has indicated that the individual differences in interpersonal skills are modulated by several genetic polymorphisms of the oxytocin receptor (*OXTR*) gene (Gong et al., 2017; He et al., 2018; Kim et al., 2010; McQuaid et al., 2015). One of the most frequently studied *OXTR* single nucleotide polymorphisms (SNPs) in the general population is rs53576. Research has indicated that compared to the A allele, the G allele of *OXTR* rs53576 is related to higher emotional sensitivity to social ostracism (McQuaid et al., 2015) and to the consequences of intentional harm (Kushner et al., 2018), as well as higher emotional social support seeking (Kim et al., 2010) and trust behavior (Krueger et al., 2012). However, the association between *OXTR* and interpersonal adaptability was not yet examined, although the associations between *OXTR* and other social skills were shown in previous studies. Overall, *OXTR* rs53576 is linked to social skills that are essential for adapting to new interpersonal interactions. It is reasonable to predict that the *OXTR* rs53576 gene will be associated with

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interpersonal adaptability in dynamic situational interactions. In this study, we investigated whether *OXTR* rs53576 polymorphism was related to individual differences in the interpersonal adaptability of college freshmen. These students had been enrolled in college for two months. Within this time window, there were diverse interpersonal demands such as coping with the difficulty of feeling at ease with others and getting along well with roommates (Fan et al., 2010; Liu, 2007). The individuals needed to monitor and adjust their actions to meet the demands of dynamic interactions. Interpersonal adaptability of freshman students taps the extent of involvement in college life (e.g., participation in extracurricular activities) and the formation and maintenance of relationships (e.g., felt quality of relationships with others; Ouyang, 2012). Thus, this ability underpins one's harmonious interpersonal relationships, life satisfaction, and psychological health (Ding, 2011; Fan et al., 2010; Zhou and Lin, 2016).

The quality of interpersonal interaction is modulated by empathy (Balconi and Vanutelli, 2017; Blanke et al., 2016; Main et al., 2017), an ability to understand and share others' internal states (Davis, 1983). Empathic abilities such as perception of social cues and the spontaneous adoption of others' viewpoints (Davis, 1983) help individuals to manage the demands of social interactions (Main et al., 2017). In this study, we were concerned with the impact of *OXTR* polymorphism specifically on empathic perception, an ability to recognize the current mental state of others. So far, previous studies have indicated that the G allele of *OXTR* rs53576 is related to higher empathic abilities as compared with the A allele (Huetter et al., 2016; Lucht et al., 2013; Rodrigues et al., 2009; Smith et al., 2014; Uzefovsky et al., 2015; Weisman et al., 2015). Moreover, our previous study (Gong et al., 2017) also indicated that the G allele of *OXTR* rs53576 is related to multi-dimensional empathy (i.e., the Perspective Taking, Fantasy, Empathic Concern, and Personal Distress subscales of the Interpersonal Reactivity Index test; Davis, 1983). However, other studies have failed to observe this association (Christ et al., 2016; Montag et al., 2012; Wu et al., 2012). In the current study we examined the relation between the *OXTR* rs53576 gene and empathic perception as measured by the Reading the Mind in the Eyes Test (RET; Baron-Cohen et al., 2001) and tested the potential mediating role that empathic perception plays in the relationship between *OXTR* and interpersonal adaptability.

Dispositional forgiveness, the ability to repair a broken social relationship calls for the wisdom seen in forgiveness, may be another mediator of association between *OXTR* rs53576 and interpersonal adaptability. Forgiveness is a prosocially psychological property that repairs transgressions in interpersonal interactions (Oostenbroek and Vaish, 2018). The disposition to forgive could regulate one's interpersonal motivations in a way that would inhibit relationship-destructive responses and promote constructive behavior toward the transgressor (Billingsley and Losin, 2017; Oostenbroek and Vaish, 2018). When freshman students from different cities and backgrounds live and study together in the new college environment, misunderstanding and conflicts might occur. To restore interpersonal harmony, the individual who has experienced transgressions must successfully manage negative emotions toward the offender (McCullough and Witvliet, 2002; Rey and Extremera, 2014). So far, although there is no experimental evidence of the causal effect of forgiveness on interpersonal adaptability, several empirical studies have indicated that individuals who frequently forgive the transgressor report less intergenerational transmission (Levenson et al., 2006) and high interpersonal adaptability (Lee and Seo, 2012). Therefore, freshmen's forgiveness is critical to interpersonal interaction after transgression (Billingsley and Losin, 2017). Previous research has also found a significant association between peripheral oxytocin reactivity and forgiveness following interpersonal harm (Tabak et al., 2011). Given the close link between oxytocin reactivity and *OXTR* rs53576 polymorphism, we predicted that dispositional forgiveness is linked to *OXTR* and may mediate the relationship between *OXTR* and interpersonal adaptability.

2. Methods

2.1. Participants

Five hundred and seventy-three full-time college freshmen (66.49% female, mean age = 19.41 ± 1.54 years; enrolled in college for two months) were recruited from Henan University of Science and Technology, China. The power analysis, conducted with G*Power 3.1, indicated that a sample of 513–779 participants was required (two-tailed $\alpha = 0.05$, $1-\beta = 0.80$) if the minimum regression coefficient of determination R^2 reaches 0.01–0.015. These college freshmen were of the majority Chinese Han ethnic group, without any known ancestors of other ethnic origins. This study was performed in accordance with the Declaration of Helsinki and approved by the Ethics Committee of Life Science College, Northwest University, China.

2.2. Interpersonal adaptability assessment

Students' interpersonal adaptability was assessed using a subscale of the Chinese revision of the Adaptability Questionnaire for Freshmen (Ouyang, 2012). The interpersonal adaptability subscale includes seven items ("Enjoys living in a dormitory; Has difficulty feeling at ease with others at college; Is satisfied with social participation; Is satisfied with social life; Gets along well with roommates; Feels that it's hard to get along with other people; Does not mix well with the opposite sex"). All of the seven items were selected from the Student Adaptation to College Questionnaire (Baker, 1986). The interpersonal adaptability subscale taps college students' interpersonal and life adjustments, particularly the extent of involvement in college life (e.g., participation in extracurricular activities) and the formation of relationships (e.g., quality of relationships with others). Given that the full-time students lived in dormitories with six to eight same-sex individuals, the item "Enjoys living in a dormitory" was used to reflect the quality of relationships with same-sex others, while the item "Does not mix well with opposite sex" was used to tap the quality of relationships with opposite-sex others. The participants indicated to what extent they agreed with each item, with 1 = almost/always false of me and 5 = almost/always true of me. In this sample, the correlation of each item with the interpersonal adaptability subscale score reached 0.710. The internal consistency measured with Cronbach's α was 0.766, similar to the value of 0.725 reported in research on the original measure (Ouyang, 2012). The mean score for interpersonal adaptability (Mean ± SD: 26.86 ± 4.25) was also comparable to the previous report (Mean ± SD = 28.89 ± 2.48, $N = 1075$; Ouyang, 2012).

2.3. Empathic perception assessment

Empathic perception was assessed with the Reading the Mind in the Eyes Test (RMET), a paper-and-pencil test that includes 36 items (Baron-Cohen et al., 2001). Each item shows a photograph displaying eye regions of a Caucasian individual along with four possible adjectives describing the current emotional or mental state of the pictured individual (Baron-Cohen et al., 2001). These adjectives were presented in written form in both the original English and in Chinese. The participants made a choice from the alternatives without time constraints. The percentage of answers that were correct (percent correct) was calculated as the score for empathic perception (Harkness et al., 2005; Maurage et al., 2011). In the study, the Cronbach's α of RMET was 0.709, which approached the value reported in our previous study (Gong et al., 2014).

2.4. Dispositional forgiveness assessment

Dispositional forgiveness was measured with the Chinese version of the 18-item Heartland Forgiveness Scale (Thompson et al., 2005). This measure provides a comprehensive index of one's dispositional

forgiveness. It consists of 18 items that measure forgiveness of self (e.g., “Although I feel bad at first when I mess up, over time I can give myself some slack”), others (e.g., “With time I am understanding of others for the mistakes they’ve made”), and situations (e.g., “With time I can be understanding of bad circumstances in my life”). For each item, the respondent makes a rating on a 7-point Likert scale, with 1 indicating “extremely disagree” and 7 indicating “extremely agree”. The Cronbach’s α was 0.791 in the current sample.

2.5. Genotyping

Genomic DNA was extracted from hair follicle cells with the Chelex-100 method. The upstream primer, 5′-ATCACTGGGTCACCTCAA-3′, and the downstream primer 5′-AACATCTGTCAGGAGCGT, were designed for polymerase chain reaction (PCR) to test the genotype of the *OXTR* rs53576 polymorphism. A 231 bp PCR fragment of this polymorphism was amplified with an initial 3 min denaturation at 94°C, followed by 35 cycles of 94°C for 30 s, 62.5°C for 35 s, 72°C for 45 s, and a final extension at 72°C for 8 min. The PCR product was incubated with restriction enzyme BamHI (FERMENTAS, MBI) overnight at 37°C. The digested fragments were identified by using 8% polyacrylamide gel electrophoresis with voltage of 200 V, followed by silver staining. The details of PCR and restriction enzyme reaction were described in our previous study (Gong et al., 2017). In this sample, the distribution of genotypes showed no deviation from Hardy-Weinberg equilibrium (AA = 262, AG = 261, GG = 50), $\chi^2 = 1.763$, $p = 0.184$.

2.6. Statistical analysis

The Hardy-Weinberg equilibrium test was conducted with the FINETTI software (Sasieni, 1997), and the power analysis was performed with G*Power 3.1 (Faul et al., 2007). When examining the genetic impacts, the linear regression analysis with genotype as predictor (0 = AA, 1 = AG, 2 = GG) was conducted with SPSS 18.0 software (SPSS Inc., Chicago, IL, USA). In the test of mediation, we bootstrapped the mediating effect using the SPSS version of the INDIRECT macro (Preacher and Hayes, 2008). The number of effective independent variables was calculated with the Matrix Spectral Decomposition (<https://neurogenetics.qimrberghofer.edu.au/matSpD/>). We assessed three outcomes associated with *OXTR* rs53576 polymorphism (interpersonal adaptability, empathic perception, and dispositional forgiveness). The variance of the eigenvalues associated with the observed outcomes was 0.634 and the number of effective independent variables was 2.577. The two-tailed significance before the Bonferroni-correction was $p < 0.019$ and this significance level was used for all analyses.

3. Results

3.1. Direct effect

A linear regression analysis with the number of G alleles as the predictor indicated that the genotype of *OXTR* rs53576 polymorphism could predict the individual differences in interpersonal adaptability, $\beta = 0.102$, $R^2 = 0.010$, $t(572) = 2.457$, $p = 0.014$, corrected $p = 0.036$. Moreover, the number of G alleles of *OXTR* rs53576 could predict the individual differences in dispositional forgiveness, $\beta = 0.107$, $R^2 = 0.012$, $t(572) = 2.583$, $p = 0.010$, corrected $p = 0.026$. By contrast, the number of G alleles of *OXTR* rs53576 could not predict the percent correct score for empathic perception after multiple adjustment, $\beta = 0.083$, $R^2 = 0.002$, $t(572) = 1.987$, $p = 0.047$, corrected $p = 0.121$. The mean \pm SD of the scores on interpersonal adaptability, empathic perception, and dispositional forgiveness were displayed in the Table 1.

3.2. Mediation analysis

The interpersonal adaptability score was significantly correlated with the dispositional forgiveness score, $r = 0.380$, $p < 0.001$, but not correlated with the empathic perception score, $r = 0.060$, $p = 0.149$. Therefore the empathic perception score was not included the mediation analysis. The empirical studies have indicated that individuals who frequently forgive the transgressor report less intergenerational transmission and high interpersonal adaptability. In this study we examined what extent dispositional forgiveness mediated the association between *OXTR* rs53576 and interpersonal adaptability.

As the direct effect analysis indicated a significant association between dispositional forgiveness and *OXTR* rs53576 polymorphism, we tested whether the association between the genotype and interpersonal adaptability was mediated by forgiveness. A regression analysis with the genotype as the predictor showed a significant relationship between *OXTR* rs53576 polymorphism and interpersonal adaptability, $\beta = 0.102$, $R^2 = 0.010$, $t(572) = 2.457$, $p = 0.014$, corrected $p = 0.036$. When both genotype and the forgiveness score were included as predictors, the effect of genotype was no longer significant, $\beta' = 0.062$, adjusted $R^2 = 0.145$, $t(572) = 1.599$, $p = 0.110$, and the difference between β and β' was significant, $F(1,570) = 79.484$, $p < 0.001$ (Neter et al., 1989). We bootstrapped the mediating effect 20,000 times (Preacher and Hayes, 2008) and found a significant mediating effect of forgiveness in the association between genotype and interpersonal adaptability, with mediating effect estimate = 0.0066, SE = 0.0046, 95% CI [0.0005, 0.0196]. As shown in the Fig. 1, the mediating effect, which was calculated with $1 - (0.062/0.102)$, accounted for 39.22% of the effect of genotype on interpersonal adaptability.

4. Discussion

This study examined the association between *OXTR* rs53576 polymorphism and individual differences in interpersonal adaptability, empathic perception, and dispositional forgiveness. The findings suggest that the G allele of *OXTR* rs53576, as compared with the AA genotype, is related to higher interpersonal adaptability and dispositional forgiveness. Moreover, dispositional forgiveness mediates the association between *OXTR* rs53576 polymorphism and interpersonal adaptability.

The *OXTR* gene has been linked to social skills that are important for forming and maintaining good social relationships. Previous studies showed that the *OXTR* rs53576 polymorphism is related to the quality of social interactions (He et al., 2018; Kim et al., 2010; Li et al., 2015; Nishina et al., 2015). Specifically, individuals with the G allele are more likely to be liked (He et al., 2018) and trusted (Nishina et al., 2015) by others as compared with individuals with the AA genotype. Moreover, individuals who carry the G allele also show increased scores on social support seeking (Kim et al., 2010), behavioral activation (Choi et al., 2018), and general sociality (Li et al., 2015). In this study, we examined the role of *OXTR* rs53576 polymorphism in the interpersonal adaptability of college freshmen. Interpersonal adaptability reflects how well college students get along with others and their satisfaction with social life at college. We assessed the interpersonal adaptability of freshmen who had been enrolled in college for only two months. During this interim, students need to actively adjust their own actions to fit the demands of new interactions. Consistent with research showing that the G allele enhances interpersonal likeability and social support seeking (He et al., 2018; Li et al., 2015; Nishina et al., 2015), individuals with the G allele show high interpersonal adaptability such as frequent extracurricular activities and high quality of relationships. It is possible that the association between the G allele and enhanced sociality contributes to the allele-dependent effect on interpersonal adaptability.

The results of previous studies indicated that the *OXTR* rs53576 polymorphism was related to individual differences in empathic perception (Baribeau et al., 2017; Lucht et al., 2013; Rodrigues et al., 2009;

Table 1
Regression analyses on the impacts of *OXTR* rs53576 on psychological outcomes.

Psychological outcomes	Means \pm SD			Statistic of regression analyses			
	AA (N = 262)	AG (N = 261)	GG (N = 50)	β	R ²	t	p
Interpersonal adaptability	26.42 \pm 4.26	27.03 \pm 4.12	27.88 \pm 4.64	0.102	0.010	2.457	0.014
Empathic perception	52.24 \pm 21.00	53.78 \pm 21.75	55.50 \pm 23.17	0.083	0.002	1.987	0.047
Dispositional forgiveness	84.99 \pm 0.68	86.36 \pm 0.68	89.38 \pm 1.51	0.107	0.012	2.583	0.010

Note: Bold font indicates significant associated statistic after Bonferroni-correction.

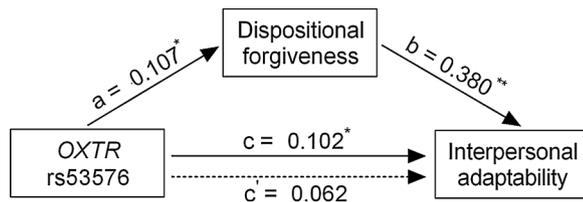


Fig. 1. The figure shows the mediation of dispositional forgiveness in the association between *OXTR* rs53576 and interpersonal adaptability. All estimates are standardized, with * indicating $p < 0.05$ and ** indicating $p < 0.01$. Note: “a” refers to the effect of *OXTR* rs53576 on dispositional forgiveness; “b” refers to the effect of dispositional forgiveness on interpersonal adaptability; “c” refers to the total effect of *OXTR* rs53576 on interpersonal adaptability; “c’” refers to the direct effect of *OXTR* rs53576 on interpersonal adaptability after controlling for dispositional forgiveness.

Weisman et al., 2015). However, the specific findings on the role of the G allele of *OXTR* rs53576 were mixed. Three studies indicated that the G allele was related to better empathic perception (Baribeau et al., 2017; Rodrigues et al., 2009; Weisman et al., 2015), while another study indicated that the G allele was related to worse empathic perception (Lucht et al., 2013). The current study indicated that the G allele of *OXTR* rs53576 did not contribute to greater empathic perception. Moreover, interestingly, empathic perception did not also link interpersonal adaptability. The association between empathic skills and social outcomes is still subject to future research.

The G allele of *OXTR* rs53576 also appears to be related to dispositional forgiveness. Engaging in a web of relationships offers both the promise of cooperative interchange and the peril of malicious exploitation. In the latter case, individuals may have continued interaction with transgressors. Studies have indicated that elevated peripheral oxytocin reactivity, but not the baseline level of oxytocin, is associated with decreased forgiveness (Tabak et al., 2011) and less forgiveness following a betrayal of trust (Yao et al., 2014). In this study, we found that dispositional forgiveness is increased as a function of the number of G alleles of the *OXTR* rs53576. Forgiveness overcomes unwanted emotional responses following interaction transgressions (Simon, 2015; Takada and Ohbuchi, 2013), with forgiveness being a function of increased empathy for the offender (Kimmes and Durtschi, 2016; McCullough et al., 1997) and related to the interpersonal motivation to produce conciliatory behavior (McCullough et al., 1997; Watkins et al., 2011). So far, studies have indicated that the G allele of *OXTR* rs53576 is related to the recovery of positive affection after stressors (Moons et al., 2014), and buffers the effect of negative social environments (e.g., interpersonal conflict; Lucas-Thompson and Holman, 2013). When navigating the difficult terrain of complex social interaction, forgiveness may serve to realize long-term benefits of continued, productive interaction, and may be contingent upon improved treatment by the transgressor. Our research extends previous studies by further demonstrating the role of *OXTR* rs53576 in individual differences in dispositional forgiveness.

In this study, we found that the association between *OXTR* rs53576 polymorphism and interpersonal adaptability was mediated by dispositional forgiveness. Previous studies indicated that individuals with the G allele were more attuned to negative social experience (Hostinar

et al., 2014) and were more able to understand and share others’ internal states, such as social distress and intention, as compared with individuals with the AA genotype. The effects of the G allele on being attuned to negative social experience and being empathic may partly contribute to individual differences in social relationships. Forgiveness plays an important role in maintaining healthy social relationships. Individuals with higher dispositional forgiveness may show greater interpersonal motivation to inhibit relationship-destructive responses and to behave constructively toward a transgressor (Billingsley and Losin, 2017; Oostenbroek and Vaish, 2018). We found that dispositional forgiveness accounted for 39.22% of the effect of genotype on interpersonal adaptability. This study provides perspective on possible pathway that dispositional forgiveness underpins the link between genetic polymorphism and interpersonal adaptability.

Several limitations must be noted. Firstly, this study was conducted with a cohort of college students who were two months into their freshman year. This cohort was selected because students making the transition to college life are likely to be in demanding social situations. Whether our findings can be extended to other groups and to other stressful social interaction situations, such as starting one’s first job, remains to be further examined. Given the robust cultural differences in social interactions, more research is needed to determine whether the observed gene-behavior relationships in this Chinese sample can be extended to other cultures, such as more individualistic western culture. Secondly, the actual effect sizes of the impacts of *OXTR* rs53576 on interpersonal adaptability, empathic perception, and dispositional forgiveness were smaller than the assumptive effect sizes. Future research with a larger cohort is needed to replicate and extend the results of the current study. Finally, the *OXTR* rs53576 polymorphism is a SNP in the third intron of the *OXTR* gene. So far, there is no direct evidence that the polymorphism of this SNP is correlated with peripheral oxytocin levels in the brain (Chang et al., 2014; Parker et al., 2014). The lack of an association between the *OXTR* rs53576 and peripheral oxytocin levels would limit the interpretation of this polymorphism as an oxytocin-related biomarker of interpersonal interactions.

5. Conclusion

This study demonstrates that the number of G alleles of *OXTR* rs53576 predicts individual differences in interpersonal adaptability and dispositional forgiveness. Moreover, dispositional forgiveness mediates the association between *OXTR* rs53576 polymorphism and interpersonal adaptability.

Declaration of conflicting interests

The authors declare that they have no conflicts of interest with respect to their authorship or the publication of this article.

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