Oxytocin Receptor Gene (OXTR) and Childhood Adversity Influence Trust

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Abstract

Early-life environments have been associated with various social behaviors, including trust, in late adolescence and adulthood. Given that the oxytocin receptor gene polymorphism (OXTR rs53576) moderates the impact of childhood experience on social behaviors, in the present study, we examined the main effect of childhood adversity through a self-report measure and its interactions with OXTR rs53576 on general trust among 203 Japanese and 200 European Canadian undergraduate students. After controlling for the effect of culture, the results indicated that childhood adversity had a negative association with general trust, and that OXTR rs53576 moderated the impact of childhood adversity on general trust. Specifically, the negative association between childhood adversity and general trust is only significant among homozygote A-allele carriers. These findings demonstrated that OXTR rs53576 moderated the relations between childhood experiences and social functioning in early adulthood.

Keywords: OXTR rs53576, childhood adversity, general trust, caution

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1. Introduction

Adverse childhood experiences can be defined as distressful events occurring in one's family or social context before late adolescence, and they are often chronic and vary in severity (Kalmakis & Chandler, 2014). Childhood experience has a significant influence on an individual's cognition and behaviors in late adolescence and adulthood. Individuals who have adverse childhood experiences, for example, engage less in prosocial behaviors in adolescence (Wu et al., 2020). Adverse childhood experiences also hinder the development of secure attachments (Afifi et al., 2011), which are extremely important for the lifelong development of trust (Bowlby, 1969). Trust is a belief that humans are benevolent in nature (Yamagishi & Yamagishi, 1994). Although little empirical research has examined the effect of childhood adversity on trusting behaviors directly, studies have indicated the negative association between disadvantaged environments and trust. Disadvantaged childhood environments are associated with faster life history strategies that are characterized by individual emphasis on immediate rewards and a lack of long-term orientation (Ellis et al., 2009; Griskevicius et al., 2011). And faster life history strategists display less trust in others (Wu et al., 2017). Additionally, socioeconomic disadvantage is also one of the important factors influencing trust. Specifically, people from families/communities of lower socioeconomic status are less trusting (e.g., Alesina & LaFerrara, 2002). Based on these findings, in the current study, we aimed to further examine the influence of childhood experience on trust.

Early life experiences have a significant influence on various aspects of an individual's lifelong development. Taking the evolutionary perspective, Belsky (1997) theorized differential susceptibility to environmental influence in children, which reflects a variation of rearing strategies to transmit one's genes in unpredictable environments.

Differential susceptibility theory suggests that individuals differ in their plasticity in a "for better or for worse" way. One of the markers of differential susceptibility is a genetic one: some people are more genetically susceptible to environmental influence (Belsky et al., 2009). People with particular genes are not only more vulnerable than others to the negative impact of adversity but also tend to benefit more from supportive and enriching experiences (Belsky & Pluess, 2009). The findings of Gene × Environment (G × E) interactions are consistent with the idea of differential susceptibility. They suggest differential susceptibility to environmental influences across the genotypes of particular genes, such as oxytocin receptor (OXTR) genes (e.g., Brody et al., 2017; Thompson et al., 2014), the 5-HTTLPR polymorphism (e.g., Caspi et al., 2003; Taylor et al., 2006), and the dopamine D4 receptor gene (e.g., Buchmann et al., 2014; Sasaki et al., 2013). In other words, individuals with environmentally sensitive genotypes are generally affected more by the external environments than others.

Extensive research has investigated the association between single nucleotide polymorphisms (SNPs) in the OXTR gene rs53576 (OXTR rs53576; adenine [A] to guanine [G] change in the third intron) and human social behaviors. In general, GG carriers exhibited more favorable social behaviors than the A-allele carriers (e.g., Kogan et al., 2011; Wu & Su, 2015). Evidence from this line of research also suggests that, when compared to men carrying the A-allele, men with GG exhibit more trust behaviors in trust games (Krueger et al., 2012) and report higher attitudinal trust (Nishina et al., 2015). However, we should be cautious in interpreting the main effect of OXTR rs53576 on human sociability. The significant relationship between OXTR rs53576 and social behaviors has not been verified through meta-analysis (Bakermans-Kranenburg & van IJzendoorn, 2014).

The G × E interactions might be one explanation for the null effect of OXTR rs53576 on sociability in the meta-analysis. Previous research established that OXTR rs53576 might

influence individual sensitivity to the social environment (Meyer-Lindenberg et al., 2011). However, for the environmentally sensitive allelic subgroup, past research on G × E interactions reported inconsistent findings. Some studies indicated that the A-allele carriers were more susceptible to the negative impacts of adversity (e.g., Van Roekel et al., 2013). In contrast, others suggested that the A-allele carriers were more resilient to the negative effect of adversity than G-allele carriers (e.g., Hostinar et al., 2014; McQuaid et al., 2013).

Little is known about how the interaction of childhood adversity and OXTR rs53576 influences the development of trust. Nevertheless, prior studies have found that OXTR rs53576 moderates the effect of childhood maltreatment on individuals' social functioning (e.g., poor or high functioning in close friendships; see Thompson et al., 2014). Early family discord increased the A-allele carriers' risk for borderline personality disorder, whereas the association between early family quality and borderline symptoms was not significant for GG carriers (Hammen et al., 2015). People with borderline personality disorder tend to exhibit less trust during interpersonal interactions (Unoka et al., 2009). Moreover, the positive association between childhood trauma and empathy for psychological pain was only significant among A-allele carriers (Flasbeck et al., 2018). Through a 4-year longitudinal study, Hygen et al. (2017) found that AA carriers' relationships with their teachers improved significantly with the enhancement of early parenting styles, whereas the student–teacher relationship was relatively stable for G allele carriers. The experience of harsh parenting in adolescence had a significant association with greater allostatic load during early adulthood only in A-allele carriers (Brody et al., 2017). Maternal postpartum depression predisposes children with the AA genotype to develop externalizing problems (Choi et al., 2019). In summary, compared with G-allele carriers, AA carriers' social functioning was more susceptible to early family life. Moreover, trust is vital for social functioning. Therefore, we hypothesized that childhood adversity could reduce an individual's trust in early adulthood

(Hypothesis 1), which might be notably stronger in AA carriers (Hypothesis 2).

To examine the influence of early family environments on trust in adulthood, in this study, we conducted a survey among Japanese and Canadian undergraduate students. We administered a generalized trust scale developed by Yamagishi and Yamagishi (1994). The scale consists of two subscales: belief in the honesty and trustworthiness of others in general (called "general trust") and cautious tendency in dealing with others (called "caution"). Caution represents people's prudence in terms of perceived risk of being exploited. Although distrustful people tend to be cautious in dealing with others (e.g., Chun & Campbell, 1974; Kaplan, 1973), because there may be cases in which even high trusters are prudent, trust and caution are not necessarily total opposites of a single dimension.

Previous evidence has suggested that collectivism was more likely to hinder general trust by comparison with individualism (e.g., Gheorghiu et al., 2009; Irwin & Berigan, 2013). Although the Japanese rated lower in general trust than the North Americans, the level of caution revealed no clear difference (Yamagishi & Yamagishi, 1994). Given the significant cross-cultural differences in general trust, in the present study, we targeted people who differ in cultural orientation (i.e., Japanese people and Canadians) and included culture as a control variable.

Although we hypothesized that childhood adversity would dent people's trust (H1), we also further examined the interactive effect of OXTR rs53576 and childhood adversity on trust. We hypothesized that the influence of adversity in early family life would be notably stronger for OXTR rs53576 AA carriers (H2). For an exploratory purpose, we also examined whether childhood adversity and the OXTR polymorphism interact with caution.

2. Method

2.1. Ethics Statement

The ethics committees at Kobe University and the University of Alberta both

approved this study. All of the participants gave a written informed consent at the beginning of the study.

2.2. Participants

We recruited 403 undergraduate students from Kobe University, Japan (98 male and 105 female, M_{age} = 19.70, SD = 1.42) and the University of Alberta, Canada (66 male, 132 female, and 2 missing, M_{age} = 19.43, SD = 2.42). According to a power analysis with the pwr package in R, we needed at least 358 participants to detect a small/medium effect size (f^2 = .04) with 80% power for an F-test with 4 numerator degrees of freedom, when the significant level was set to 0.025 (= 0.05/2 tested hypotheses) based on the Bonferroni correction. We excluded data from 2 participants who did not complete the measurement of childhood adversity and 38 whose genotypes were undetermined; therefore, the final sample size was 363.

2.3. Self-Report Measures

2.3.1. Childhood Adversity

We assessed childhood adversity using the Risky Families Questionnaire (RFQ) (Taylor et al., 2004). We asked respondents to rate their early family environment in terms of 13 aspects on a 5-point Likert scale (1 = not at all, 5 = very often). The items assessed family conflict, abuse, neglect, and disorganized households in childhood (ages 5 to 15). Sample items included, “How often did a parent or other adult in the household make you feel that you were loved, supported, and cared for?” (a positively worded item) and “How often did a parent or other adult in the household push, grab, shove, or slap you?” Two Japanese–English bilinguals translated and back-translated the items between Japanese and English to ensure cross-cultural equivalence. We averaged the ratings for the items with reverse coded positively worded items. Higher scores represented more adverse childhood environments. For nonclinical samples, the scores of RFQ in previous work on the G × E interactions ranged roughly from 1.00 to 4.23 (e.g., Carver et al., 2011; Carver et al., 2016). The

distributions of the current samples (Japanese: range = 0.85–3.62, Median = 1.92; Canadians: range = 1.00–4.31, Median = 2.00) were similar to those reported in prior work. The Cronbach's alpha coefficients for the current sample were .76 for the Japanese and .86 for the Canadians.

2.3.2. General Trust and Caution

In this study, we used the 5-item General Trust Scale (GTS; Yamagishi et al., 2015) and the 5-item Caution Scale (CS), both originally developed by Yamagishi and Yamagishi (1994). We asked the respondents to rate their agreement with each item on a 7-point Likert scale (1 = strongly disagree, 7 = strongly agree). Sample items included "Most people are trustworthy" (GTS), and "There are many hypocrites in this society" (CS). The Cronbach's alphas of the GTS were .74 for the Japanese and .80 for the Canadians. The Cronbach's alphas of the CS were .60 for the Japanese and .74 for the Canadians.

2.4. Genotyping

We extracted genomic DNA from nail samples using ISOHAIR kits (Nippon Gene Co., Ltd., Tokyo, Japan). We genotyped the SNP marker for OXTR rs53576 in the same way as Ishii et al. (2020) did. Each SNP assay contained forward and reverse polymerase chain reaction (PCR) primers and two allele specific probes conjugated with either the VIC or the FAM fluorescent marker. Each PCR mixture consisted of DNA templates, the SNP-specific Genotyping Assay, and the Taqman Genotype master mix (Thermo Fisher Scientific Inc.). We performed all PCR and allelic discrimination reactions on the StepOne Plus™ Real-Time PCR System (Thermo Fisher Scientific Inc.).

3. Results

3.1. Genotype Distribution

Consistent with previous studies showing that A-allele carriers are more often Asians than individuals of European ancestry (e.g., Luo & Han, 2014), the distribution of OXTR

rs53576 genotypes was significantly different between the Canadians (18 AA, 84 AG, 76 GG, 22 undetermined) and the Japanese (70 AA, 77 AG, 40 GG, 16 undetermined; $\chi^2(2) = 42.01$, $p < .001$). The distribution of the allele frequencies for the Canadian sample fell in the Hardy-Weinberg equilibrium ($\chi^2 = 0.56$, $p = .507$). However, for the Japanese sample, the distribution deviated slightly from the Hardy-Weinberg equilibrium (the heterozygotes were less frequent than expected; $\chi^2 = 4.48$, $p = .035$).

The results of the correlational analyses (Table 1) showed that risky families scores correlated with general trust negatively ($r(361) = –.22$, $p < .001$), whereas the correlation between risky families scores and caution was not significant ($r(361) = .10$, $p = .067$). Additionally, general trust correlated with caution negatively ($r(361) = –.43$, $p < .001$). The results of the one-way ANOVAs indicated that participants with different OXTR genotypes did not significantly differ in risky families scores ($F(2, 360) = 2.97$, $p = .053$, $\eta^2 = .016$), general trust ($F(2, 360) = 0.15$, $p = .857$, $\eta^2 = .001$), or caution ($F(2, 360) = 0.35$, $p = .707$, $\eta^2 = .002$). The mean scores by OXTR genotype appear in Table 2.

3.2. Gene x Childhood Environment Interaction

We formulated a series of multiple regression analyses to examine the moderating effect of OXTR rs53576 on the association of childhood adversity with general trust and caution. Before conducting the regression analyses, we dummy coded the OXTR genotypes: we used the AA genotype as the reference category, and two dummy-coded variables were (0, 1, 0) and (0, 0, 1) for (AA, AG, GG). Risky families scores were mean-centered as indicators of childhood adversity. In the hierarchical multiple regression analysis, we tested for the main effects of childhood adversity and the two OXTR dummy-coded variables first. This model also included gender (male = 0, female = 1) and culture (Japanese = 0, Canadian = 1) as potential control variables (Step 1). Then, we entered the interactions with the two OXTR dummy-coded variables and the risky families scores in Step 2.

3.2.1. General Trust

The multiple regression analyses (Table 3) showed there was no difference in general trust between the AA and AG/GG carriers (*p*s > .458). After controlling for the effect of culture and gender, the main effect of childhood adversity was significant in Step 1 ($b = -0.34$, $SE = 0.08$, $t(356) = -4.36$, $p < .001$), which showed that childhood adversity reduced general trust significantly. However, the influence of childhood adversity on general trust differed significantly between the AA and AG carriers ($b = 0.81$, $SE = 0.21$, $t(354) = 3.87$, $p < .001$). Moreover, the influence of childhood adversity on trust also differed significantly between the AA and GG carriers ($b = 0.78$, $SE = 0.22$, $t(354) = 3.53$, $p < .001$). The childhood adversity and gene interactions were not qualified by culture (Table S1). A simple slope analysis showed that childhood adversity reduced the AA carriers' trust ($b = -0.98$, $SE = 0.18$, $t(354) = -5.59$, $p < .001$; Figure 1a) significantly, whereas it did not significantly predict the AG ($b = -0.18$, $SE = 0.11$, $t(354) = -1.62$, $p = .106$; Figure 1b) or the GG carriers' trust ($b = -0.21$, $SE = 0.13$, $t(354) = -1.56$, $p = .119$; Figure 1c) in early adulthood.

3.2.2. Caution

In the analyses of caution (Table 4), the main effect of childhood adversity was not significant in Step 1 ($b = 0.14$, $SE = 0.08$, $t(356) = 1.91$, $p = .057$). There was not any significant difference in caution between the AA and AG/GG carriers (*p*s > .176). However, the influence of childhood adversity on caution differed somewhat between the AA and AG carriers ($b = -0.43$, $SE = 0.20$, $t(354) = -2.13$, $p = .034$). The difference on the influence of childhood adversity between the AA and AG carriers was not qualified by culture (Table S2). The influence of childhood adversity on caution did not differ significantly between the AA and GG carriers ($b = -0.30$, $SE = 0.22$, $t(354) = -1.41$, $p = .160$). Further analyses showed that childhood adversity increased the AA carriers' caution significantly ($b = -0.45$, $SE = 0.17$, $t(354) = -2.62$, $p = .009$; Figure 2a), whereas the association between childhood adversity

and caution was not significant for the AG carriers (b = –0.02, SE = 0.11, t(354) = 0.17, p = .868; Figure 2b) or the GG carriers (b = –0.15, SE = 0.13, t(354) = –1.15, p = .251; Figure 2c).

4. Discussion

The primary aim of the present study was to examine the influence of early family environments on people's trust in early adulthood. Specifically, we examined whether childhood adversity would reduce trust. Based on studies demonstrating that the impact of early life experience on social functioning in late adolescence and adulthood varies across different genotypes on OXTR rs53576 (e.g., Flasbeck et al., 2018), we also aimed to test whether OXTR rs53576 would moderate the influence of childhood adversity on people's trust. Consistent with Wu et al.'s (2020) work, even after controlling for the effect of culture, we found a main effect of adverse childhood experience on general trust. More importantly, the results supported our moderation hypothesis that the impact of childhood adversity on general trust in early adulthood was only significant for the OXTR rs53576 AA carriers, not the G-allele carriers. Specifically, adverse childhood experience reduced the OXTR rs53576 AA carriers' general trust significantly, whereas the negative impact of childhood adversity on general trust was not significant for the G-allele carriers.

We also examined the effect of childhood adversity and its interaction with OXTR rs53576 on caution exploratorily. The results demonstrated that neither the main effect of childhood adversity nor its interactions with OXTR rs53576 on caution were significant. Nevertheless, the influence of childhood adversity on caution among the AA carriers was slightly stronger than that among the AG carriers. Specifically, childhood adversity only increased the AA carriers' caution significantly in early adulthood. We also found a significant cross-cultural difference in caution. By comparison with the Canadians, the Japanese were more prudent in dealing with others.

These results extend previous work on the development of trust in several important ways. First, the current study is one of the first to directly examine the influence of childhood experiences on general trust. Faster life history strategies from disadvantaged childhood environments lead individuals to emphasize their immediate self-interests and to display a lack of long-term orientation. Moreover, such individuals are vulnerable to others' exploitative behaviors, specifically in scarce-resource environments. The vulnerability, then, would make it harder for them to trust others. Importantly, the current findings also provide evidence that positive interactions with caregivers during early life are particularly important for the development of general trust (Bowlby, 1969). Future studies could use longitudinal designs to examine the influence of early-life experience on trusting behaviors further. Additionally, as a positive bias in cognition, trust is an essential prerequisite for living in relationships with other people. Trust involves one's expectations for others' benevolent intentions; it boosts cooperation, particularly in situations that include conflict between self-interest and collective interest (Balliet & Van Lange, 2013); and it relates to one's ability to discern cooperative partners from uncooperative ones (Yamagishi et al., 1999). Future studies could also investigate how childhood experience influences prosocial behaviors and one's ability to detect trustworthiness—and how trust underlies the influences of childhood experience.

Second, the current findings add evidence for research suggesting that OXTR rs53576 moderates the effect of early-life experience on social functioning (e.g., Cicchetti et al., 2014; Senese et al., 2019). Our results suggest that the significant impact of childhood adversity on general trust is only limited to AA carriers. According to the gene-environment interaction (Obradović & Boyce, 2009), we speculate that, compared with the OXTR rs53576 G allele carriers, the AA carriers are more susceptible to family environmental influence, at least in regard to trust. A recent study found an interactive effect of OXTR rs53576 and early

emotional trauma on left hippocampal volumes (Malhi et al., 2020). Specifically, the left hippocampal volumes of adolescent girls suffering higher emotional trauma during childhood were smaller than those of others, which was only evident among AA carriers (Malhi et al., 2020). The hippocampus is an important region that contributes to reinforcement learning apart from the striatum (Davidow et al., 2016). The reinforcement learning circuitry was also part of the establishment of trust (Fareri et al., 2012). Prior work on faster life strategies suggested that people favoring immediate rewards also were less trusting (Wu et al., 2017). Together with the current findings, we speculate that the increased sensitivity to childhood adversity in people with the AA genotype on hippocampal volumes might also explain the same effect on trust. For OXTR rs53576 AA carriers, childhood adversity might disrupt the function of reward circuits by influencing the left hippocampal volumes, thus impacting their trusting behaviors. Future studies could investigate this possibility further.

However, to date, the findings on the environmentally sensitive allelic subgroup of OXTR rs53576 are mixed. Some researchers have suggested that the association between childhood experiences and emotional function (e.g., emotional regulation) was much stronger among GG carriers than A-allele carriers (e.g., Bradley et al., 2011; Burkhouse et al., 2016). These discrepancies might be due to gender, ethnicity, types of adversity, and outcome variables. By using a cross-cultural sample, in the present study, we specifically focused on young adults, early family environments, and trust. Future studies could clarify whether the environmentally sensitive allelic subgroup of OXTR rs53576 varies in its outcomes in psychological domains (e.g., personality traits and socioemotional processes). Besides OXTR rs53576, previous studies have found that other polymorphisms of the OXTR gene also moderated the effects of early experiences on people's cognitions and behaviors. For example, Apter-Levy et al. (2013) found that OXTR rs2254298 moderated the association between children's mental health and family environment. Thus, we speculate that the inconsistent

results for the environmentally sensitive allelic subgroup of OXTR rs53576 might be explained by gene–gene interactions. Therefore, future work needs to investigate further whether other polymorphisms of the OXTR gene (e.g., OXTR rs2254298) are involved in the G × E interaction on general trust.

Another possible explanation for this G × E interaction on general trust is that, compared with AA homozygotes, the OXTR rs53576 G-allele carriers might be more capable of developing their general trust outside their own families. Previous studies have suggested that the G-allele was connected to higher levels of psychological resources (Saphire-Bernstein et al., 2011) and higher openness to social support (Chen et al., 2011). Therefore, when the family environment is unfavorable, it might be much easier for the G-allele carriers to learn social skills from other social supports (e.g., friends, teachers). That might be the reason why the association between early family environments and general trust was weaker among the G-allele carriers than among AA carriers. In short, our findings supported the idea that it is important to consider the influence of specific genes when examining the impact of early life experience on later social life.

Finally, our research also contributed to the evidence on the cross-cultural differences in general trust and caution. Consistent with previous studies suggesting that individual cultures fostered trust among people (Gheorghiu et al., 2009), the Canadians were more likely than the Japanese to trust others. Additionally, our findings also suggested that the Japanese were more cautious in dealing with others than the Canadians. Although Yamagishi and Yamagishi (1994) neither expected nor found a clear cultural difference in caution between the Japanese and the North Americans, the current finding could be interpreted through cultural differences in vigilance to others' negative feelings (e.g., Adams, 2005; Hashimoto & Yamagishi, 2016; Ishii et al., 2011). In collectivistic cultures in which people exist in a network of strong ties, to avoid exclusion from the current network, it is crucial for individual

survival to be sensitive to others' expectations and not offend them.

There are several limitations that should be noted in this study. First, the distribution of the OXTR rs53576 allele frequencies for the Japanese sample violated the Hardy-Weinberg equilibrium slightly. For some unknown reason, we sampled heterozygotes less than expected (77 observed heterozygotes vs. 91 expected sample size). Future studies need to follow the random sampling procedure more strictly to examine further the interactive effect of OXTR rs53576 polymorphism × childhood adversity on trust. However, it is noteworthy that this study demonstrated a significant main effect of childhood adversity and its significant interaction with OXTR rs53576 on trust across cultures. Second, the current study measured trust only through a self-reported measurement. Therefore, it is still unclear whether the significant G × E interaction we found is applicable to people's trust in practical situations.

In conclusion, the current study demonstrated that OXTR rs53576 moderated the impact of childhood adversity on general trust. Overall, more childhood adversity predicted lower general trust. This effect was particularly true among carriers of AA homozygotes. These findings contribute to the understanding of the ways in which gene and early family environments influence people's trust interactively in their later lives.

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Table 1

Descriptive statistics and correlations (N = 363)

Scale	Mean	*SD*	1	2	3
1. Risky families	2.04	0.63	1.00		
2. General trust	4.21	0.95	-.22**	1.00	
3. Caution	4.73	0.90	.10	-.43**	1.00

Note. ** $p < .001$.

Table 2

Means by OXTRrs53576 genotype

	AA (*N* = 88)		AG (*N* = 159)		GG (*N* = 116)			
Scale	Mean	*SD*	Mean	*SD*	Mean	*SD*	*F*	*p*
1. Risky families	1.91	0.55	2.05	0.66	2.13	0.64	2.97	.053
2. General trust	4.23	1.05	4.23	0.90	4.17	0.95	0.15	.857
3. Caution	4.71	0.83	4.69	0.92	4.78	0.95	0.35	.707

Table 3

Results of multiple regressions predicting general trust.

	Step 1 (R^2 = .065, p < .001)				Step 2 (ΔR^2 = .042, p < .001)			
Predictors	*b*	*SE*	*t*(356)	*p*	*b*	*SE*	*t*(354)	*p*
Gender (0: M, 1: F)	-0.11	0.10	-1.08	.280	-0.10	0.10	-0.97	.332
Culture (0: Jpn, 1: Can)	0.26	0.10	2.45	.015	0.26	0.10	2.49	.013
Childhood adversity	-0.34	0.08	-4.36	<.001	-0.98	0.18	-5.59	<.001
*OXTR*1 (0: AA, 1: AG)	-0.04	0.13	-0.30	.766	0.04	0.13	0.34	.732
*OXTR*2 (0: AA, 1: GG)	-0.10	0.14	-0.74	.458	-0.03	0.14	-0.24	.813
Childhood adversity × *OXTR*1					0.81	0.21	3.87	<.001
Childhood adversity × *OXTR*2					0.78	0.22	3.53	<.001

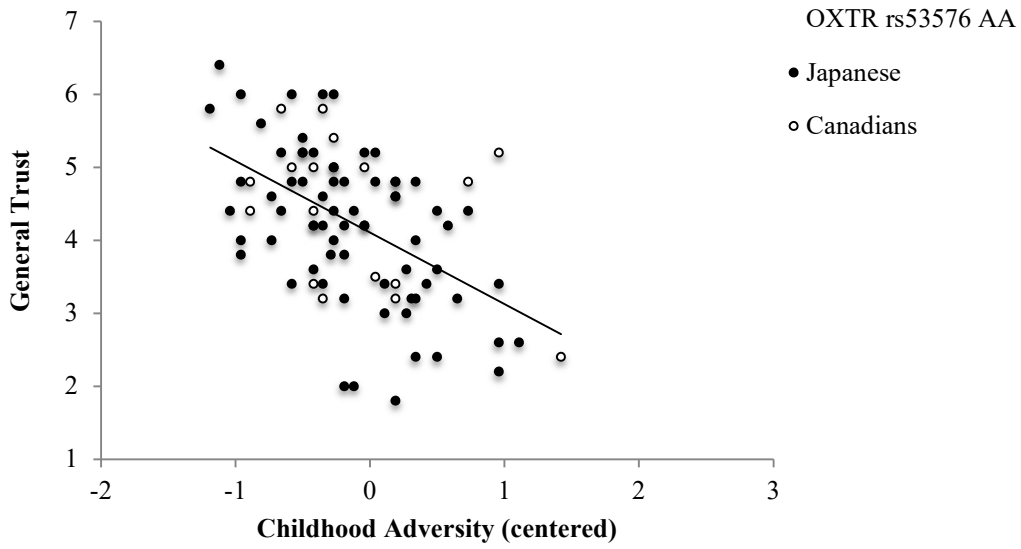
Table 4

Results of multiple regressions predicting caution.

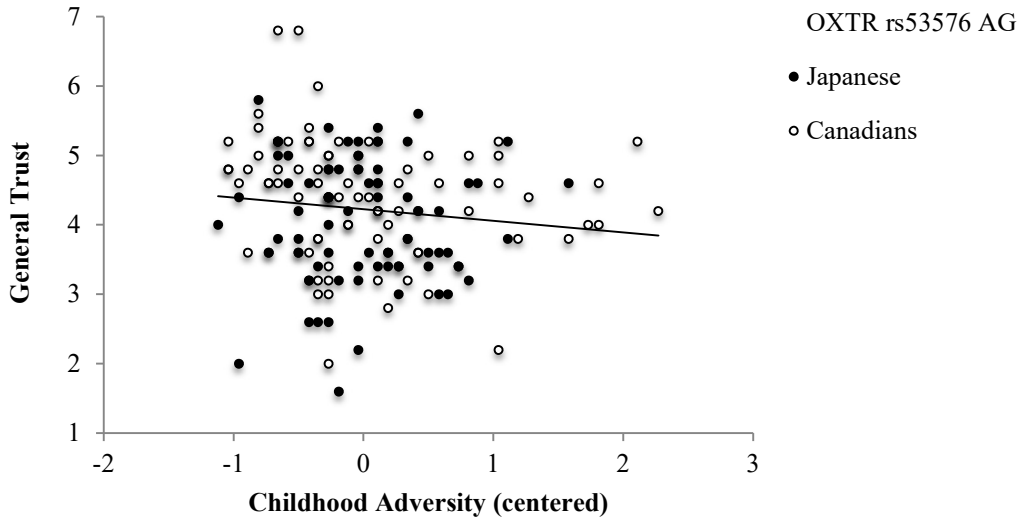
	Step 1 (R^2 = .047, p = .004)				Step 2 (ΔR^2 = .012, p = .104)			
Predictors	*b*	*SE*	*t*(356)	*p*	*b*	*SE*	*t*(354)	*p*
Gender (0: M, 1: F)	-0.13	0.10	-1.41	.161	-0.14	0.10	-1.50	.135
Culture (0: Jpn, 1: Can)	-0.32	0.10	-3.14	.002	-0.32	0.10	-3.14	.002
Childhood adversity	0.14	0.08	1.91	.057	0.45	0.17	2.62	.009
*OXTR*1 (0: AA, 1: AG)	0.07	0.12	0.55	.586	0.03	0.12	0.23	.819
*OXTR*2 (0: AA, 1: GG)	0.18	0.13	1.36	.176	0.14	0.14	1.05	.294
Childhood adversity × *OXTR*1					-0.43	0.20	-2.13	.034
Childhood adversity × *OXTR*2					-0.30	0.22	-1.41	.160

Figure 1a-1c

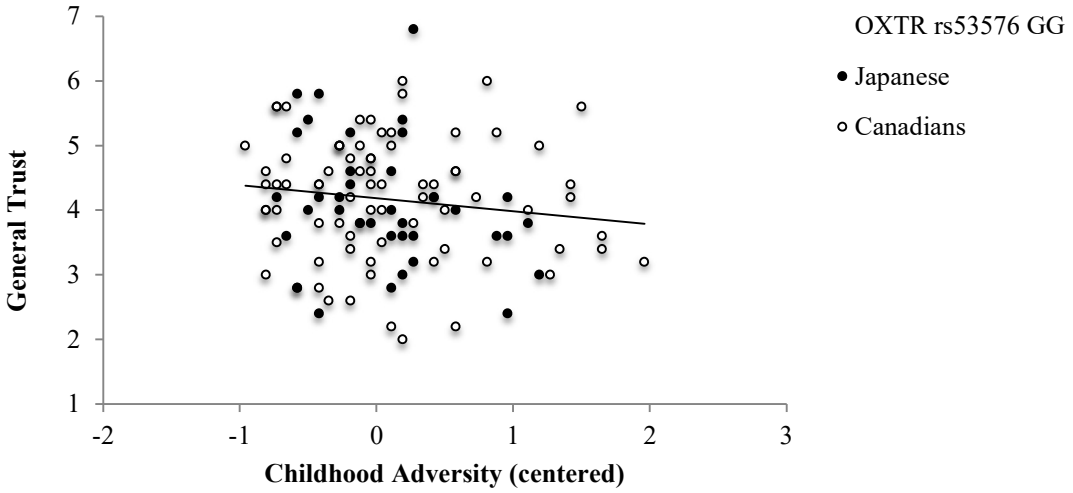
General trust as a function of childhood adversity by OXTR rs53576 genotype.



(Figure 1a)



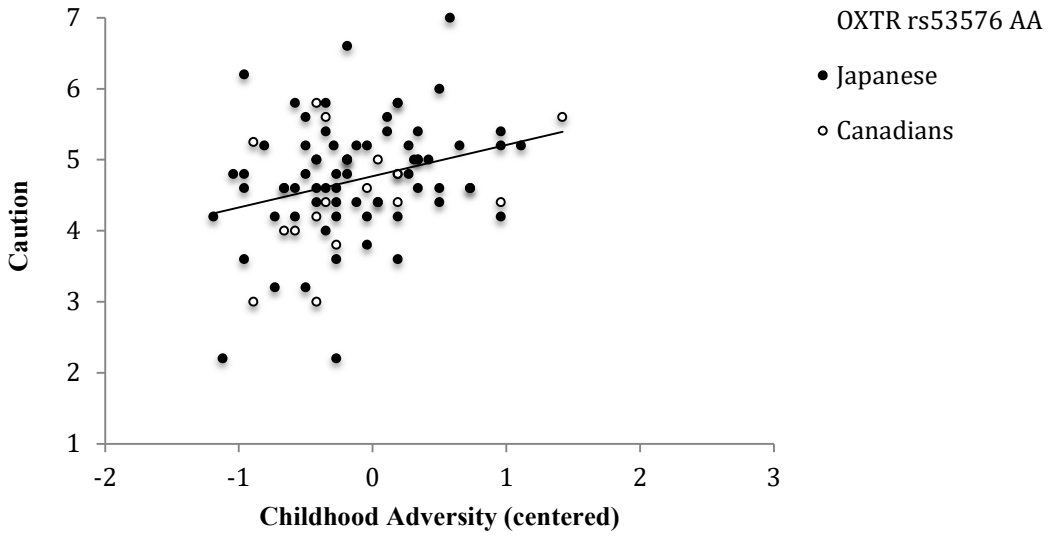
(Figure 1b)


General Trust
7
6
5
4
3
2
1
-2
-1
0
1
2
3
Childhood Adversity (centered)
OXTR rs53576 GG
Japanese
Canadians

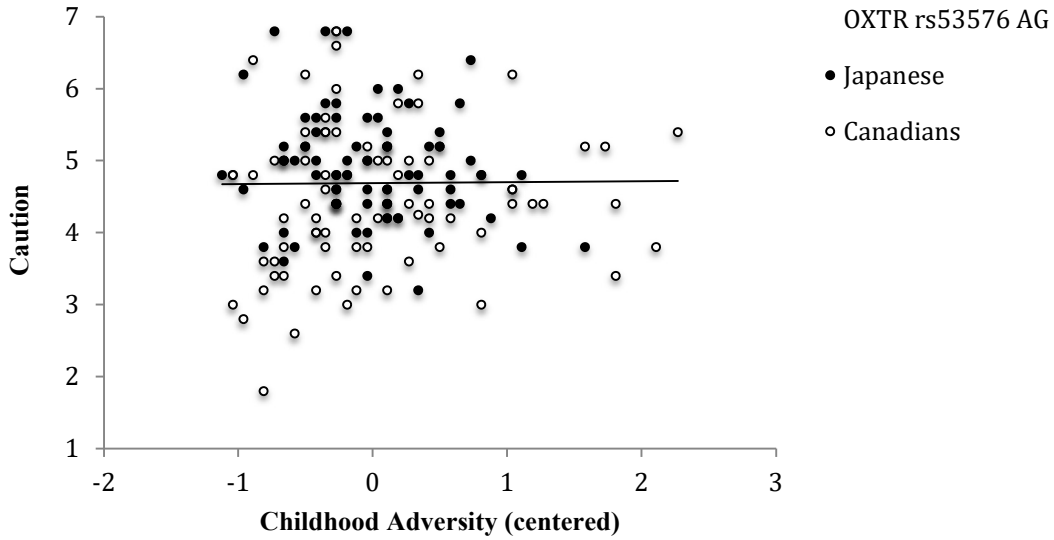
(Figure 1c)

Figure 2a-2c

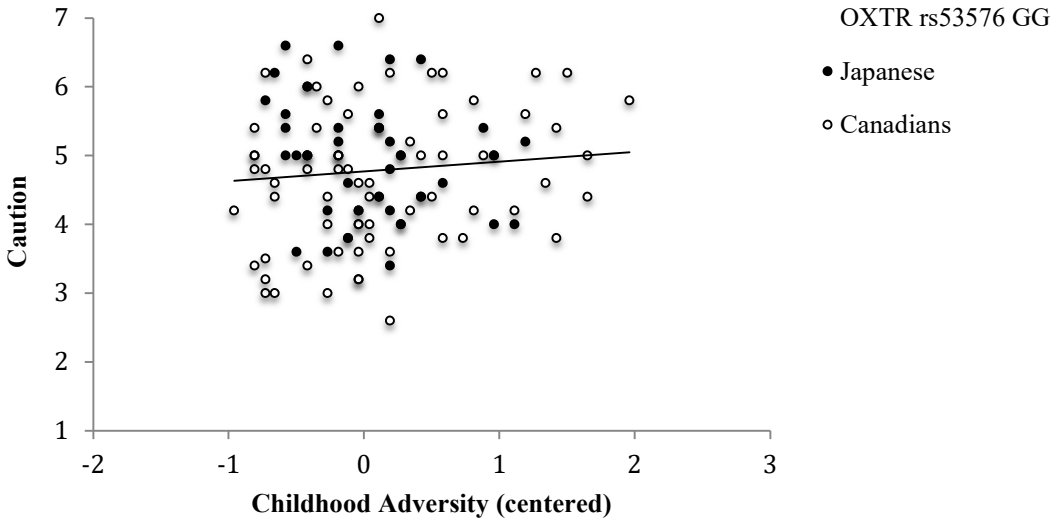
Caution as a function of childhood adversity by OXTR rs53576 genotype.



(Figure 2a)



(Figure 2b)


OXTR rs53576 GG
Japanese
Canadians
Caution
Childhood Adversity (centered)
7
6
5
4
3
2
1
-2
-1
0
1
2
3

(Figure 2c)

Supplementary Analyses

The main effect of culture was also significant in the multiple regression models, which might raise another interesting question. That is whether culture moderates the interaction between OXTR rs53576 gene and childhood adversity. To further clarify the effect of culture, based on the previous models, we added the interaction between culture and childhood adversity, the interaction with culture and two OXTR dummy codes, and the three-way interactions in step 3. However, the results showed that any effect including culture was not significant (*p*s > .153). The changes in R-square from Step 2 to Step 3 were not significant (*p*s > .098). More importantly, the significant interaction between OXTR and childhood adversity remained (*p*s < .046). The results of multiple regressions are summarized in Table S1 and Table S2.

Table S1

Results of interactions including culture predicting general trust.

	Step 3 (ΔR^2 = .008, p = .683)			
Predictors	*b*	*SE*	*t*(349)	*p*
Gender (0: M, 1: F)	-0.09	0.10	-0.93	.353
Culture (0: Jpn, 1: Can)	0.33	0.24	1.36	.173
Childhood adversity	-1.11	0.20	-5.45	<.001
OXTR1 (0: AA, 1: AG)	0.05	0.15	0.31	.755
OXTR2 (0: AA, 1: GG)	0.05	0.18	0.28	.777
Childhood adversity × OXTR1	1.04	0.29	3.66	<.001
Childhood adversity × OXTR2	0.69	0.34	2.00	.046
Culture × Childhood adversity × OXTR1	-0.67	0.47	-1.42	.158
Culture × Childhood adversity × OXTR2	-0.22	0.51	-0.43	.668
Culture × Childhood adversity	0.51	0.41	1.25	.212
Culture × OXTR1	-0.04	0.28	-0.14	.890
Culture × OXTR2	-0.17	0.30	-0.57	.570

Table S2

Results of interactions including culture predicting caution.

	Step 3 (ΔR^2 = .025, p = .098)			
Predictors	*b*	*SE*	*t*(349)	*p*
Gender (0: M, 1: F)	-0.17	0.10	-1.80	.073
Culture (0: Jpn, 1: Can)	-0.25	0.24	-1.05	.294
Childhood adversity	0.45	0.20	2.28	.023
OXTR1 (0: AA, 1: AG)	0.07	0.15	0.44	.657
OXTR2 (0: AA, 1: GG)	0.15	0.18	0.86	.388
Childhood adversity × OXTR1	-0.74	0.28	-2.66	.008
Childhood adversity × OXTR2	-0.85	0.33	2.56	.011
Culture × Childhood adversity × OXTR1	0.44	0.46	0.96	.336
Culture × Childhood adversity × OXTR2	0.72	0.50	1.43	.153
Culture × Childhood adversity	0.00	0.40	0.00	.999
Culture × OXTR1	-0.12	0.27	-0.42	.672
Culture × OXTR2	-0.06	0.29	-0.21	.835