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Gene–culture interaction: influence of culture and oxytocin receptor gene (*OXTR*) polymorphism on loneliness

Jessica LeClair¹ · Joni Y. Sasaki² · Keiko Ishii³ · Mizuho Shinada⁴ · Heejung S. Kim¹

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Abstract Previous research has shown that culture and genes can interact to influence social behaviors. Variation of the oxytocin receptor gene (*OXTR*) rs53576 polymorphism has been linked to differential susceptibility to cultural influences with genetically susceptible individuals showing more culturally typical behaviors. The present research focuses on a psychological outcome of such behaviors, specifically loneliness, which is an outcome related to well-being. We also considered attachment style as a mediator for the interaction between culture and *OXTR* genetic variation on loneliness. Previous gene–culture interaction research shows that G-allele carriers may be genetically predisposed to show more culturally typical behaviors and psychological tendencies, compared to A-allele carriers. Thus, we expected that genetically susceptible Japanese would show a more avoidant attachment style (a pattern more common in Japan), while susceptible Americans would show a more secure attachment style (a pattern more common in the U.S.). In both cultures, we expected that greater avoidant relationship tendencies would predict greater loneliness. Participants (217 American and 153 Japanese students) completed scales to measure loneliness and attachment style, and provided saliva for genotyping. As predicted, culture moderated the link between genetic susceptibility and loneliness, with G-allele Americans showing less loneliness than A-allele carriers. Further, the link was mediated by attachment style. Our study

✉ Jessica LeClair
jessica.leclair@psych.ucsb.edu

✉ Heejung S. Kim
heejung.kim@psych.ucsb.edu

¹ UC Santa Barbara, Santa Barbara, USA

² York University, York, UK

³ Kobe University, Kobe, Japan

⁴ Tokyo Gakugei University, Tokyo, Japan

extends existing research by showing that gene–culture interactions on relationship patterns have consequences for psychological well-being outcomes.

Keywords Culture · Loneliness · Attachment · Genetics · Cultural neuroscience

Introduction

Relationships with others form a central part of everyday life. Indeed, the desire for interpersonal relationships has been proposed as a fundamental human need (Baumeister and Leary 1995). While relationships form a fundamental part of human experience, there is a growing body of evidence revealing rich diversity in how interpersonal relationships are established, maintained, and practiced across cultures (e.g., Adams 2005; Kim et al. 2008; Schug et al. 2010). The implications for well-being of such cultural differences in relationship patterns have not well studied. Further, existing research has not fully considered both culture and individual differences, which taken together can contribute to an integrated understanding of within- and between-culture differences (Cohen and Leung 2010; Leung and Cohen 2011). In the present research, we aimed to address these current limitations by considering the individual difference factor of genetic variation, set within the context of sociocultural differences in interpersonal relationship processes, and to examine the implications for outcomes related to well being.

Previous research has found that carriers of genetic variants, associated with increased susceptibility to environmental influences, show tendencies more in line with their cultural surroundings. For example, genetically susceptible individuals show more culturally consistent tendencies of self-expression, emotion suppression, and social orientation (Kim et al. 2010a, b, 2011; Kitayama et al. 2014; LeClair et al. 2014; Luo et al. 2015). While the interactive influence of culture and genes has been relatively well-established, most of these studies have only considered culturally variant behavioral tendencies as outcomes. In the present study, we extend such investigations by looking at relational well-being, an important psychological consequence of behavioral differences. Indeed, the question of how genes, in conjunction with cultural factors, impact outcomes related to psychological well-being is virtually unknown. The present study examines the gene–culture interaction on a relational well-being outcome, namely loneliness, which is an important risk factor for compromised health and well-being (Hawkley and Cacioppo 2010). More specifically, we look at how a variant (*rs53576*) of the oxytocin receptor gene (*OXTR*) is associated with loneliness in three groups: European Americans, Asian Americans, and Japanese. We examine the role of cultural differences in relationship patterns by considering attachment style as a potential mediator.

Cultural differences in relationships

Across cultures, there exist culturally specific patterns of interpersonal relationships. Such differences, especially between North American and East Asian cultures, have been well documented (e.g., Kitayama and Uchida 2005; Mesquita and Ellsworth

2001; Morling et al. 2003) and are theorized to arise from cultural differences in how people view the self (Markus and Kitayama 1991). In individualistic cultures, like the United States, an independent view of the self is dominant, which emphasizes the self as autonomous, independent, and possessing a set of stable internal attributes that guide behavior. Relationships, while important, are relatively more changeable and viewed as freely chosen with fewer obligations (Adams and Plaut 2003; Schug et al. 2010). In contrast, in collectivistic cultures, like Japan, the dominant interdependent view of the self conceptualizes the self as connected, bound to others, and flexible based on situations. Relationships form a central element of the interdependent self, which is defined by the relationship of the self to others (Hamaguchi 1985). In these cultures, interpersonal relationships are viewed as less voluntary (Adams 2005).

These differences have implications for how individuals engage with their interpersonal relationships. Compared to individuals from individualistic cultures, individuals from collectivistic cultures tend to be more motivated to adjust to the expectations of others (Morling et al. 2002) and are particularly attuned to rejection or possible negative evaluation from close others. Research has shown that East Asian individuals are more sensitive to cues of interpersonal disapproval (Ishii et al. 2011), experience more interpersonal worries (e.g., Hoshino-Browne et al. 2005; Kitayama et al. 2004), feel greater stress trying to avoid and minimize the likelihood of upsetting others (Hashimoto et al. 2012), and are more cautious in disclosing their personal problems when seeking social support from close others (Kim et al. 2008).

We propose that the cultural differences described above closely relate to attachment style (Bowlby 1969; Hazan and Shaver 1987). Attachment style, proposed as a model of child and caregiver attachment and responses (Bowlby 1969), has been extended to adult relationships by focusing on individual differences in attachment anxiety and attachment avoidance (Hazan and Shaver 1987). Given the greater interpersonal worry and relational concern among East Asians, we expect that East Asians would show less secure attachment, which would explain increased feelings of loneliness. Further, attachment style has been shown to predict loneliness with secure attachment negatively associated with perceived levels of loneliness (Deniz et al. 2005; DiTommaso et al. 2003; Wiseman et al. 2006). Thus, we expect the less secure attachment among East Asians would explain increased feelings of loneliness.

Existing research provides support for our expectation that cultural differences in interpersonal relationships will be reflected in attachment style. Overall Japanese adults score higher on both attachment anxiety and avoidance compared to American adults (Ishii et al. 2011). Further, comparing between Japan and the United States, valued ways of caring for children in Japan, namely fostering emotional closeness and dependency, reflect insecure attachment, while valued ways of caring for children in the United States support more secure attachment (Rothbaum et al. 2000). These findings support the idea that the cultural context and typical relational concern of East Asians is more consistent with an insecure attachment style.

In particular, the dimension of attachment avoidance, representing the degree of discomfort felt towards getting close to and relying on partners, relates to social

support seeking, which has been shown to vary across cultures (see Kim, et al. 2008 for a review). Compared to individuals from North American cultures, individuals from East Asian cultures show greater reluctance to seek social support, especially emotion-focused social support as opposed to problem-focused support (Chen et al. 2012). In previous research, variation of the oxytocin receptor gene (*OXTR*) has been found to interact with culture to predict social support seeking with genetically susceptible East Asians less likely to seek support compared to European Americans (Kim et al. 2010a). Such research focused on coping responses to a specific and recent stressor. Building on these findings, in the current research, we focus on the attachment style as a measure of more general relationship patterns, which may predict overall feelings of loneliness. In other words, we focus on attachment style as a culture-specific relationship pattern from which a particular type of social support use arises. Therefore we consider insecure attachment style, both anxious and avoidant tendencies. Given evidence showing that avoidant attachment predicts lower levels of social support seeking (Florian et al. 1995; Ognibene and Collins 1998), we particularly focus on avoidance attachment style as a potential mediator related to loneliness.

Gene–culture interaction framework

Research has shown that genetic factors and external environmental factors can interact to influence behavioral and psychological outcomes, highlighting certain genes as ‘plasticity genes,’ which confer increased susceptibility to the environment (e.g., Belsky et al. 2009; Belsky et al. 2007). Specifically, the gene–environment ($G \times E$) framework proposes that environmental conditions can moderate the phenotypic manifestation of the genotype (Caspi et al. 2002, 2003). For example, individuals carrying the S-allele of the 5-*HTTLPR* polymorphism show a stronger link between exposure to adverse life events and later depressive symptoms compared to those without it (Caspi et al. 2003; and see Karg et al. 2011 for meta-analysis). The framework has produced consistent findings across a number of genes, such as the dopamine D₄ receptor (*DRD4*) gene (Bakermans-Kranenburg and Van IJzendoorn 2006, 2011; Sasaki et al. 2013), the monoamine oxidase-A (*MAOA*) gene (Caspi et al. 2002; Foley et al. 2004; Kim-Cohen et al. 2006), and the oxytocin receptor (*OXTR*) gene (Chen et al. 2011).

While $G \times E$ research focuses predominantly on the ‘environment’ as differing forms of individual experience, the gene–culture interaction ($G \times C$) framework expands the notion of ‘environment’ to include aspects of the sociocultural context. Culture is defined as comprising a mutually shared system of beliefs and values that define norms and practices (Kitayama et al. 2002; Markus and Kitayama 1991). Culturally typical tendencies tend to be magnified in individuals carrying susceptibility variants. A number of papers provide evidence for the $G \times C$ framework, including interaction effects between culture and oxytocin receptor gene (*OXTR*) variation on emotional support seeking (Kim et al. 2010a) and emotion suppression (Kim et al. 2011), serotonin 1A receptor gene (*5HTT1A*) variation on holistic attention (Kim et al. 2010b), serotonin transporter

polymorphism (*5-HTTLPR*) variation on facial expression detection (Ishii et al. 2014), and dopamine D₄ receptor (*DRD4*) variation on social orientation (Kitayama et al. 2014). Moreover, variation of the *OXTR* rs53576 polymorphism has been found to interact with interdependence, a key variable distinguishing East Asian and Western cultures, to predict empathy (Luo et al. 2015). Such G×C studies have highlighted the role of susceptibility to cultural influences of ‘plasticity’ genes, by showing that variation of such genes predispose an individual to exhibit more culturally typical patterns of behavior and psychological tendencies (see Kim and Sasaki 2014 for a review).

In the present study, we focus on a polymorphism in the oxytocin receptor gene (*OXTR*), a gene that has been implicated in social affiliation behaviors. The specific rs53576 single-nucleotide polymorphic site has been linked to differences in amygdala activation and in structural changes in the hypothalamus region (Tost et al. 2010). Carriers of the G-allele of *OXTR* rs53576 tend to show more sensitive parenting behavior (Bakermans-Kranenburg and Van IJzendoorn 2008), greater responsiveness to infant crying (Riem et al. 2011), more empathic accuracy (Rodrigues et al. 2009), and more susceptible to environment cues to be prosocial (Sasaki et al. 2015; see also Li et al. 2015 for a meta-analysis). Further, previous G×C research has implicated this specific variant in cultural susceptibility to affiliation behaviors, such as social support seeking (e.g., Kim et al. 2010a). For example, *OXTR* rs53576 variation was found to moderate cultural differences in emotional support seeking, such that Americans carrying the susceptibility variant (i.e., G-allele) reported more emotional support seeking (consistent with an American cultural context in which social coping is fostered), while Koreans reported less emotional support seeking (again consistent with an East Asian cultural context in which social coping is discouraged) (Kim et al. 2010a). How individuals engage close others in the time of distress are closely related to attachment styles (Collins and Feeney 2000). Considering these findings together, we predicted that we would find a G×C interaction on loneliness and that attachment style would mediate this interaction.

Present work

The present study aims to test the G×C model on a proposed psychological outcome of culturally variant tendencies, namely loneliness, as mediated by attachment style (but see also Gillath et al. 2008). Specifically, we examined the interaction between the *OXTR* rs53576 polymorphism and culture (i.e., American and Japanese participants) in influencing reported feelings of loneliness. We predicted that feelings of loneliness would differ between cultures based on findings that Japanese tend to be more concerned with interpersonal conflict and more careful with interpersonal interactions (Hashimoto et al. 2012). We suggest that among Americans, the decreased relational concern might lead to less caution about expanding social networks, and may relate to objectively larger social networks, or at least an experience of less isolation and loneliness among Americans, compared to Japanese.

Further, we examined whether the link between the gene by culture interaction and loneliness would be mediated by attachment style (Bowlby 1969; Hazan and Shaver 1987). We propose that the typical relational concern of Japanese is more consistent with an insecure attachment style, and thus attachment style might explain the link between the interaction of culture and genetic susceptibility on loneliness.

We predicted a $G \times C$ interaction on loneliness based on variation of the selected *OXTR* polymorphism. Consistent with previous $G \times C$ research, we assumed that GG-Americans and GG-Japanese (i.e., those carrying the susceptibility variant) would be more predisposed to follow culturally normative relationship patterns, compared to AA-Japanese and AA-Americans.

Among Americans, we predicted that G-allele carriers would exhibit less loneliness, consistent with an American culture context that places less emphasis on interpersonal caution. In contrast, we expected that Japanese would show the opposite pattern with G-allele carriers exhibiting higher loneliness compared to those without the G-allele, a pattern consistent with a Japanese cultural context in which interpersonal caution is emphasized.

Further, we predicted that attachment style would mediate the link between underlying genetic variation and loneliness. We expected that GG-Japanese would show a more insecure relationship pattern, while GG-American would show a more secure relationship pattern. Our model assumes that the link between insecure relationship tendencies and loneliness is not moderated by culture or by *OXTR* variation. Rather, we propose that across cultures, as an individual develops a certain relationship pattern, loneliness will be related in the same way. In other words, we suggest that a more insecure relationship style will be linked with greater feelings of loneliness across both cultural contexts.

Additionally, in the present study, a subset of American participants was Asian American. Utilizing the method that was used in previous research (e.g., Kim et al. 2010a, 2011), we also conducted additional analyses to investigate whether the gene–culture interaction was driven by cultural exposure, by specifically examining the association among Asian Americans. We predicted that Asian Americans, who are biologically more similar to the Japanese but have greater exposure to American culture, would show a pattern of results in between the other two groups. In other words, given their exposure to American culture, the pattern of Asian Americans would begin to resemble the pattern of European Americans.

Method

Participants

Participants included 153 Japanese undergraduates (61 % female) and 218 American undergraduates (63 % female; 67 % European American). Asian American and European American participants were recruited in the United States based on their self-categorized ethnicity. Of the Asian Americans, 68 % were East Asian, including from China, Japan, and South Korea, 36 % were from Southeast

Asia, including from Cambodia, the Philippines, and Vietnam, and <1 % were from India. Among the Asian Americans, 69 % were born in the United States, and the remaining 31 % were born outside of the United States. All of the Asian Americans went to high school in the United States, showing that they had lived in the United States for at least several years. Japanese participants were recruited in Japan on the basis of birth country and name at recruitment. Participants were recruited through the psychology department participant pool and class announcements. For participation, participants received either course credit or monetary compensation (10 U.S. dollars or 1000 Japanese yen respectively).

Procedure and materials

As part of a larger collection of questionnaires, participants completed the following measures on a computer: the Loneliness Scale (Russell et al. 1978) and the Adult Attachment Scale (Fraley et al. 2000). The Loneliness Scale includes 20 items that assess the extent to which participants feel loneliness and social isolation on a 1(*never*) to 4(*often*) scale ($\alpha_{\text{U.S.}} = .927$ and $\alpha_{\text{Japan}} = .875$) with higher scores indicating greater loneliness. Example items include, “*I feel left out*” and “*I lack companionship.*” The Adult Attachment Scale includes a total of 36 items in sets of 9 items that relate to a specific attachment figure, including mother, father, dating partner, and friend. The items assess individual differences in two attachment dimensions: anxiety ($\alpha_{\text{EuropeanAmerican}} = .608$, $\alpha_{\text{AsianAmerican}} = .852$, and $\alpha_{\text{Japanese}} = .724$ and avoidance ($\alpha_{\text{EuropeanAmerican}} = .856$, $\alpha_{\text{AsianAmerican}} = .804$, and $\alpha_{\text{Japan}} = .813$), on a scale from 1(*strongly disagree*) to 7(*strongly agree*).¹ There are 6 items related to anxiety, for example, “*I often worry that my [mother figure] does not care for me*” and three items related to avoidance, for example, “*I prefer not to show my [mother] how I feel deep down.*” All measures were originally developed in English and translated into Japanese using the back-translation method. After the questionnaires, participants completed basic demographic items and provided saliva samples for genotyping.

Genotyping

Saliva samples were collected with the Oragene collection device (Genotek). Per manufacturer recommendations, the samples were kept at room temperature prior to DNA extraction. DNA was extracted following recommendation from manufacturer (DNA Genotek, Ontario, Canada). DNA was quantitated using A260/A280 ratio, and OXTR was identified using the following protocol. The OXTR-C__3290335_10 was genotyped using a 5' nuclease assay to discriminate between the two alleles (Taqman SNP Genotyping Assay OXTR-C__3290335_10, Applied Biosystems Inc.). Polymerase chain reactions were performed using 5- μ L reaction volumes in 384-well plates with 5 ng of DNA. The standard protocol provided with

¹ Across all three cultural groups, there was a positive correlation between attachment avoidance and anxiety, $r_{\text{European Americans}}(145) = .403$, $p < .001$, $r_{\text{Asian Americans}}(72) = .306$, $p = .009$, $r_{\text{Japanese}}(153) = .431$, $p < .001$.

the kit was followed. End point reads of fluorescence levels were obtained with an ABI 7900HT Sequence Detection System. To assign the score associated with the *OXTR* genotypes, we utilized an additive model (Lewis 2002; Minelli et al. 2005), which assumes a linear monotonic relationship between environmental susceptibility and copies of the relevant allele. In other words, the most susceptible homozygote based on existing literature was assigned a value of 2 (i.e., GG genotype), the heterozygote a value of 1 (i.e., AG genotype), and the theoretically least susceptible homozygote a value of 0 (i.e., AA genotype).

Results

Consistent with previous studies using fully independent samples (e.g., Chang et al. 2014; Kim et al. 2010a), we found significant differences in the distributions of the *OXTR* polymorphism alleles comparing among European Americans, Asian Americans, and Japanese. Among European Americans, there was a higher proportion of G alleles (12 A/A, 61 A/G, 64 G/G, and 8 lacking genotype data), while among Asian Americans and Japanese, there was a higher proportion of A alleles (Asian Americans: 24 A/A, 36 A/G, 9 G/G, and 3 lacking genotype data; Japanese: 59 A/A, 67 A/G, 21 G/G, and 6 lacking genotype data), $\chi^2(4, N = 353) = 62.485, p < .001$. For all three groups, the distributions did not violate the Hardy–Weinberg equilibrium expectation, $\chi^2(2, N = 137) = .22, p > .89$ for European Americans, $\chi^2(2, N = 69) = .63, p > .73$ for Asian Americans, and $\chi^2(2, N = 147) = .08, p = .96$ for Japanese (Rodriguez et al. 2009). When comparing across the three groups (i.e., European Americans, Asian Americans, and Japanese), we found a consistent pattern for mean-levels of loneliness and attachment avoidance with Asian Americans showing patterns in between European Americans and Japanese (see Table 1).

To examine the overall cultural and genetic differences in feelings of loneliness, as well as the interactive effect comparing Americans (European Americans and Asian Americans) to Japanese, we conducted a 2 (culture: American vs. Japanese) by 3 (*OXTR*: AA vs. AG vs. GG) analysis of variance (ANOVA). Comparing the

Table 1 Comparing European Americans, Asian Americans, and Japanese on loneliness and attachment avoidance

Variable	Group	N	Mean	SE	One-way ANOVA
Loneliness	EA	145	1.68	.039	$F(2, 367) = 28.51, p < .001$
	AA	72	1.80	.055	
	JPN	153	2.10	.038	
Avoidance	EA	145	2.78	.076	$F(2, 367) = 13.94, p < .001$
	AA	72	3.05	.108	
	JPN	153	3.44	.074	

two cultural groups, there was a significant main effect of culture with Japanese participants reporting greater loneliness ($M = 2.11$, $SE = .043$) compared to American participants ($M = 1.73$, $SE = .035$), $F(1, 347) = 45.930$, $p < .001$. As expected, there was no significant main effect of *OXTR* variation, $F(2, 347) = .500$, $p = .607$; however, there was a significant interactive effect between culture and *OXTR* variation, $F(2, 347) = 4.110$, $p = .017$.² American participants carrying two copies of the susceptibility variant of *OXTR* reported less loneliness ($M = 1.59$, $SE = .054$) compared to those completely lacking the susceptibility variant ($M = 1.84$, $SE = .077$), $p = .007$. Among Americans, the heterozygote AG-genotype individuals reported greater loneliness ($M = 1.77$, $SE = .047$) than GG-individuals ($p = .01$) but did not report less loneliness than AA-individuals ($p = .45$). Inconsistent with our predictions, we found no relationship between *OXTR* variation and loneliness among Japanese. Japanese GG-genotype individuals ($M = 2.21$, $SE = .101$) did not show greater loneliness compared to AA-genotype individuals ($M = 2.08$, $SE = .060$), $p = .267$. In addition, heterozygote AG-genotype individuals in Japan did not report significantly higher loneliness ($M = 2.04$, $SE = .056$) compared to either GG-genotype Japanese ($p = .13$) or AA-genotype Japanese ($p = .60$) (See Fig. 1).

In addition to comparing Americans and Japanese to explore the gene–culture interaction on loneliness, we conducted additional analyses comparing Asian Americans versus European Americans, and Asian Americans versus Japanese. We were interested in whether Asian Americans showed patterns more similar to European Americans or Japanese to explore the effect of biological similarity versus cultural exposure explanations. We predicted that based on exposure to American cultural contexts, Asian Americans would show patterns more similar to European Americans evidenced by a nonsignificant gene–culture interaction on loneliness when directly comparing the two American groups. Similar to the main analyses, we ran two separate 2 (culture) by 3 (*OXTR*: AA vs. AG vs. GG) analyses of variance (ANOVA's). In the first, we included a culture variable coded to compare European Americans to Asian Americans. We found no main effect of culture, $F(1, 200) = .025$, $p = .874$, and as predicted, no significant gene–culture interaction, $F(2, 200) = .367$, $p = .693$. In the second analysis, comparing Asian Americans to Japanese, we found a significant main effect of culture, $F(1, 210) = 26.304$, $p < .001$, with Asian American participants reporting less loneliness ($M = 1.72$, $SE = .063$) compared to Japanese participants ($M = 2.11$, $SE = .042$). Further, we found a marginally significant gene–culture interaction, $F(2, 210) = 2.817$, $p = .062$. These analyses provide evidence that Asian Americans results resemble the pattern of European Americans more than the pattern of Japanese. Thus, these results support our suggestion that the gene–culture interaction is indeed driven by cultural experiences, rather than other unmeasured factors.

² Controlling for gender does not alter the significance of the interaction.

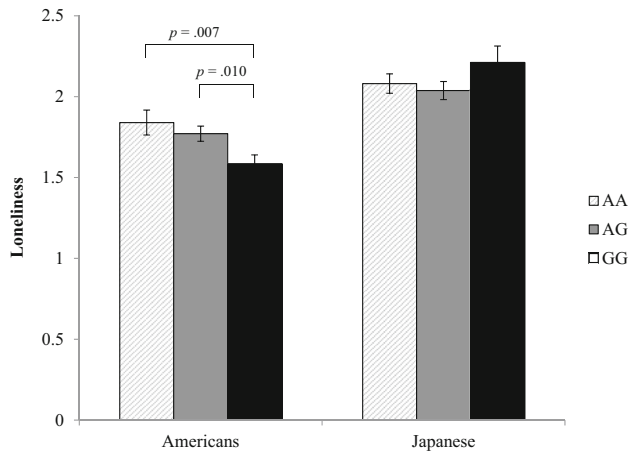


Fig. 1 Loneliness by culture and *OXTR* variation. (Note Error bars show standard errors. Significant within-culture pairwise comparisons are marked)

Mediational analyses

To test the effects of attachment avoidance, we ran separate mediational analyses considering both attachment avoidance and attachment anxiety as potential mediator. We found that attachment avoidance, but not anxiety, mediated the link. For avoidance, the results indicated that the total effect of the $G \times C$ interaction on loneliness [$\beta = .202$, $t(349) = 2.443$, $p = .015$] was reduced when attachment avoidance was included in the model [$\beta = .142$, $t(348) = 1.835$, $p = .067$]. The effect of the $G \times C$ interaction on attachment avoidance was marginally significant [$\beta = .169$, $t(349) = 1.961$, $p = .051$] and attachment avoidance [$\beta = .355$, $t(348) = 7.441$, $p < .001$] significantly predicted feelings of loneliness. Using PROCESS, indirect effects were computed for 1000 bootstrapped samples and 95 % confidence intervals were computed (Hayes 2012). The analyses revealed that the indirect effect was significant for attachment avoidance (indirect effect = .052, 95 % CI [.0040, .1117]). (See Fig. 2). We did not find any mediating relationship with attachment anxiety.

Discussion

Summary

In the present study, we found the predicted interactive effect between sociocultural context and variation of the selected *OXTR* polymorphism on loneliness. For Americans exposed to a cultural context in which relationships are viewed as flexible and requiring less careful behavior, carriers of the susceptibility *OXTR* variant exhibited less loneliness compared to non-carriers. The interaction was

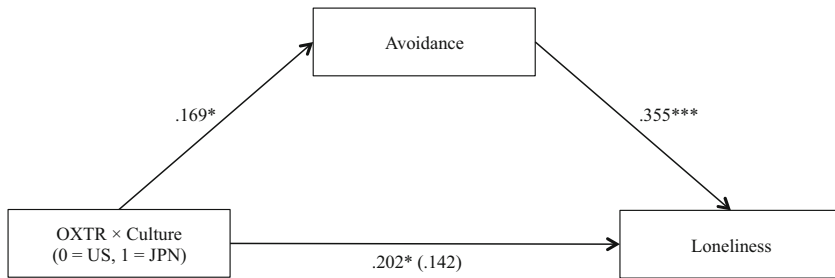


Fig. 2 Attachment avoidance as mediator of link between G×C interaction and loneliness. (Note Path coefficients show standardized coefficients. * $p < .05$, ** $p < .01$, *** $p < .001$)

mediated by attachment style, specifically the avoidance dimension, which is related to caution in interpersonal contexts. Further, when comparing between Asian Americans and European Americans (versus the comparison between Asian Americans and Japanese) we found no evidence of an interaction, providing support for the importance of cultural exposure. More than biological similarity, it was the pattern of exposure to cultural environments that predicted the G×C interaction.

Psychological consequences of being culturally consistent

Our approach of considering a psychological outcome of cultural differences, rather than the behavior itself, has a number of important methodological and theoretical strengths. In terms of methodology, we used attachment style to capture between-culture differences in interpersonal relationships. As predicted, attachment avoidance mediated the relationship of the gene–culture interaction on loneliness. In future work, including attachment style, as we did in the present study, could help move beyond simply documenting behavioral differences in the context of interpersonal relations to capturing the underlying psychological mechanisms. Our findings for the relationship between variants of the *OXTR* gene and culture with attachment style may appear inconsistent with previously published work, which showed a lack of association (Gillath et al. 2008). However, we also found a lack of direct association between *OXTR* variation and attachment style. It was only when accounting for the interaction with sociocultural context that the relationship between the genetic variant and specifically attachment avoidance emerged. Further, our additional analyses with Asian Americans contribute to highlighting cultural influence as the key element helping to explain the gene–culture interaction. Comparing groups based on cultural exposure (i.e., between Americans and Japanese), we found the predicted interaction between genetic variation and sociocultural factors; however, we found no interaction when comparing groups based on biological similarity (i.e., European Americans versus Japanese and Asian Americans).

While it is often found that fitting into cultural surroundings has positive benefits (e.g., De Leersnyder et al. 2014; Fulmer et al. 2010), our findings suggest that it may not always be beneficial to exhibit dominant cultural tendencies, depending on the

nature of those tendencies. Perhaps some psychological tendencies, like experiencing concern and caution towards interpersonal relationships, may not bring psychological benefits even if they are normative in a given cultural context. Another explanation is that the subjective measure of loneliness used in our study may capture subjective perceptions of social networks, rather than reflecting objective qualities of actual networks. Although previous research finds that perceived support matters more than objective support availability or received support (Wethington and Kessler 1986), the relative importance of subjective versus objective support itself may vary across cultures. Therefore, it could be that although Japanese report subjectively feeling greater loneliness, in fact their social networks are objectively strong. Thus their objective support system may serve as a buffer against negative health outcomes. In the current study, we did not include an objective measure of social networks. Future work could include such a measure to examine how subjective loneliness relates to actual networks and to psychological outcomes.

Based on the present findings, another possibility is that, like being a racial minority confers risks for certain negative experiences, being a genetic minority could increase the risk for certain negative outcomes. We found that in America, where the susceptibility variant of the *OXTR* gene is relatively more common, susceptibility carriers exhibit less loneliness, perhaps reflecting a benefit of being in the genetic majority. In contrast, susceptibility carriers in Japan (i.e., the genetic minority group) did not show any greater loneliness. Therefore, it may be possible that being in a genetic majority offers psychological benefits, perhaps by conferring increased sense of belongingness to their cultural group. However, the genetic minority explanation does not fully account for the mediational role of attachment style, as we found in the present study.

Consistent with previous work, we found ethnic variation in the allelic distribution of *OXTR*, with the susceptible G-allele appearing more commonly among Americans compared to Japanese. Culture–gene coevolution proposes that adaptive cultural tendencies may evolve to influence the social and physical environment in which evolution occurs (Boyd and Richerson 1985; Chiao and Blizinsky 2010). According to this perspective, the population distribution of *OXTR* distribution could be related to underlying cultural values themselves. For example, researchers found that across 12 nations, the A-allele frequency of *OXTR* positively correlates with collectivistic cultural values (Luo and Han 2014). Given that the A-allele predicts symptoms of depression and anxiety (Saphire-Bernstein et al. 2011), cultural values of collectivism may serve as an adaptation to protect otherwise genetically susceptible populations against mental health disorders. In our results, perhaps the collectivistic structure in Japan helped to buffer the susceptible A-allele carriers against greater loneliness.

Limitations and future directions

There are several limitations to the study. The sample size is relatively small and the interactive effect sizes are modest. In particular, the nonsignificant effect of *OXTR* among Japanese may be explained by the small sample size. Although we did not

expect that the link between relationship patterns and loneliness would vary as a function of culture, it is possible that the social consequence of being avoidant in Japan differs from the United States. In Japan, where avoidant relationship tendencies are more culturally normative, perhaps the effect on loneliness is not as strong, providing an alternative explanation for the lack of increased loneliness among genetically susceptible Japanese showing a more avoidant attachment style. Further the current study is based on variation of a single gene. While we acknowledge that it is unlikely a single gene determines a psychological tendency like environmental susceptibility (LeClair et al. 2014), it is important to note that *OXTR* in the present study conceptually replicated the basic pattern of previous findings (Kim et al. 2010a, 2011; Sasaki et al. 2015). Future studies could consider biological relationships between single genes in order to choose sets of genes that more fully and reliably capture the brain systems involved. Additionally, we did not measure specific cultural value orientations but rather used country background as a proxy for such values. Given that countries may differ on a variety of values, we acknowledge the potential imprecision of this approach. Future work should more fully account for such variety of differences by analyzing the interaction between specific cultural traits and genetic variation as some researchers have recently begun to do (e.g., Luo et al. 2015; Ma et al. 2013).

In the present research, we built upon previous research showing that culture and genes can interact to influence social behaviors. We considered a potential psychological outcome of such culturally variant social behaviors, namely loneliness. Our findings illustrate the importance of considering how gene–culture interactions on behavioral and psychological tendencies, like relationship patterns, may have consequences for well-being across cultures.

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Compliance with ethical standards

Conflict of Interest The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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