Serotonin Receptor (*HTR2A*) Gene Polymorphism Modulates Social Sharing of Happiness in Both American and Japanese Adults

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Abstract

A single nucleotide polymorphism in the serotonin 2A receptor gene (*HTR2A*rs6311 guanine [G] vs. adenine [A]) appears associated with positive emotional contagion (social sharing of happiness) in Japanese people. However, it remains unknown whether the *HTR2A* polymorphism also impacts the social sharing of happiness in Western cultures. The present study thus compared 207 Japanese university students and 200 American adults (including non-students). Social sharing of happiness was examined using a vignette-based questionnaire. Participants were asked to imagine that they were experiencing an emotionally neutral event. At the same time, they were asked to imagine that a friend was experiencing a positive valence event (presence condition), whereas in the other condition such information was not presented (absence condition). Results showed that the G allele carriers felt happier in the presence than in the absence of the friend compared with participants with the AA genotype. Although we did not specifically consider comparability between the two samples, the findings suggest that the effect of *HTR2A*polymorphisms on social sharing of happiness observed in Japanese populations may be applicable to American populations.

Subjective well-being is a broad, multifaceted, and complex construct that comprises the global evaluation of the overall positivity of each individual's life, as well as the balance of their positive and negative affective states (Diener, **1984**; Hudson, Lucas, & Donnellan, **2020**). Thus, psychologists emphasize that subjective well-being includes at least two separate components: global and experiential well-being. Global well-being is evaluative and refers to the overall appraisals of people on how well their lives are going (overall life satisfaction). In contrast, experiential well-being refers to the actual, in vivo, affective state of each individual, and is considered a state comprising ephemeral positive feelings or a lack of negative feelings (Berridge & Kringelbach, **2011**; Schimmack, **2008**). Global and experiential well-being are partially interactive. Although the level of global well-being is relatively stable within individuals (such as trait-like features), it may change within a relatively short time in response to various external emotional factors (Otake, Shimai, Tanaka-Matsumi, Otsui, & Fredrickson, **2006**; Schimmack, **2008**; Seligman, Steen, Park, & Peterson, **2005**). Some researchers have distinguished the concept of “well-being”

from "happiness" (Raibley, **2012**); however, the concept of happiness also has trait-like and state-like aspects, similar to global and experiential well-being (Matsunaga et al., **2016**). We deem that happiness and well-being can be partially interchangeable, and happiness can serve as a "proxy" for well-being (Raibley, **2012**). Thus, in this study we used the term *happiness* as an interchangeable term for *well-being*.

Previous studies have indicated that the emotional state is strongly influenced by the presence of companions (Doherty, Orimoto, Singelis, Hatfield, & Hebb, **1995**; Hatfield, Cacioppo, & Rapson, **1993**; Wagner et al., **2015**). As personal relationships are filled with experiences of hedonic events, including praise or kindness received from others (Kawamichi, Tanabe, Takahashi, & Sadato, **2013**; Otake et al., **2006**), positive social relationships are considered one of the most important modulators of subjective well-being (Hudson et al., **2020**; Saphire-Bernstein & Taylor, **2013**). In a previous study that tested how experiential effects vary as a function of the specific people currently present, participants reported that the level of experiential well-being is high in the company of their friends, romantic partners, and children (Hudson et al., **2020**). Additionally, the study demonstrated that the company of romantic partners positively influences the level of global well-being. Furthermore, a previous study indicated that the presence of a happy person enhances the happiness of others; therefore, positive feelings are contagious (social sharing of positive emotions and happiness; Fowler & Christakis, **2008**).

Recent studies have demonstrated that genetics may also influence the experiential well-being (state-like aspect of happiness) that accompanies social relationships through the human ability of empathy (Matsunaga et al., **2017**, **2018**). It was reported that the single nucleotide polymorphism (SNP) adenine (A)-1,438 guanine (G) (rs6311) in the serotonin (5-hydroxytryptamine, 5-HT) 2A receptor gene (*HTR2A*) is associated with the social sharing of happiness (Matsunaga et al., **2017**). G-allele carriers of *HTR2A* rs6311 were reported to experience happier feelings during empathy than did individuals with the AA genotype (such as in the case of friendships, where friendships have not changed, but the friend has made new and reliable friends and deepened their ties with them recently; Matsunaga et al., **2017**). Given that previous research implicates the serotonin system in empathic ability (Dolder, Schmid, Müller, Borgwardt, & Liechti, **2016**), *HTR2A* polymorphisms are associated with the effect of sharing happiness by modulating the human ability to empathize.

Genetics and culture appear to be interactive (Chiao & Blizinsky, **2010**). For instance, the culture–gene coevolutionary theory proposes that cultural traits are adaptive, evolving, and influencing the social and physical environments under which genetic selection operates (Boyd

& Richerson, **1985**). Chiao and Blizinsky (**2010**) have previously examined the association between cultural values of individualism–collectivism and the allelic frequency of a serotonin transporter functional (*5-HTTLPR*) polymorphism, which is associated with serotonergic neurotransmission. They reported that the increased population frequency of the *5-HTTLPR* short allele, which is associated with increased negative emotion including heightened anxiety, predicts a decreased prevalence of anxiety and mood disorders across nations owing to increased collectivistic cultural values. Additionally, a previous study explored the effect of gene polymorphisms in serotonin 1A receptor (*HTR1A*) on the modes of thinking (locus of attention; H. S. Kim, Sherman, Taylor et al., **2010**). It is known that there are differences in modes of thinking between people from Eastern and Western cultures (Nisbett, Peng, Choi, & Norenzayan, **2001**), with holistic thinking (the tendency to attend to the entire field) being more prevalent in Eastern cultural contexts, whereas analytic thinking (the tendency to attend primarily to focal information) is more prevalent in Western cultural contexts. Using a battery of questionnaires, H. S. Kim, Sherman, Taylor, et al. (**2010**) reported a significant interaction between the SNP cytosine (C)-1,019 guanine (G) (rs6295) in *HTR1A* and culture regarding the locus of attention (meaning, "it is more important to pay attention to the whole context rather than the details"). Although Americans with the G allele, which is considered to be associated with reduced serotonin transmission, show increased attention to the focal object, Koreans with the G allele show increased attention to the context (H. S. Kim, Sherman, Taylor, et al., **2010**). However, the underlying mechanisms by which low 5-HT activity leads to different responses among different cultures has not been clarified. It is possible that the 5-HT system is linked to the degree to which people adhere to psychological tendencies that are modal and reinforced in their cultural contexts.

As the previous study that explored the effect of *HTR2A* on social sharing of happiness only included people within Eastern cultures (Japanese culture; Matsunaga et al., **2017**), it remains unclear whether the effect of *HTR2A* on social sharing of happiness is also prevalent in Western cultures, such as within American populations. Although prior findings indicate cultural differences in self-reported empathy (Melchers, Li, Chen, Zhang, & Montag, **2015**), research on Western–Eastern cross-cultural differences in self-reported empathy is limited (Melchers et al., **2016**, **2015**). Using a questionnaire-based approach, a previous study examined adolescents from three ethnic groups in China (Han, Jingpo, and Dai); although there were differences in emotional processes between them—Dai people dance and express happiness after the death of a relative, Jingpo people dance and chant the achievements of the dead to reduce the pain of the close relatives of the dead, and Han people cry and express sadness—the positive emotional contagion similarly affects their positive mood states (Kuang, Peng, Xie, & Hu, **2019**). Thus, it is

possible that the effect of *HTR2A* on social sharing of happiness is similar between Western and Eastern cultures. Therefore, in the present study, we recruited not only Japanese individuals but also Americans to further evaluate whether the effect of *HTR2A* polymorphisms on social sharing of happiness is applicable to populations from different cultures.

Materials and Methods

Participants

To investigate the gene–culture interaction in the social sharing of happiness, we recruited 207 Japanese undergraduate students (95 men and 112 women, mean age ± standard deviation [M_{age}] = 19.85 ± 1.41 years, range = 18–25 years) and 200 residents living in the Chicago area (IL, USA; 106 men, 92 women, and 2 missing entries for gender, M_{age} = 29.86 ± 14.16 years, range = 18–86 years). The Japanese students were recruited through a psychology subject pool in Nagoya University (year in school and university division of the participants were variable). American residents were recruited through the subject pool in the Center for Decision Research of the University of Chicago in downtown Chicago. This study was approved by the Ethics Committees of Aichi Medical University, Nagoya University, Kobe University, and the University of Chicago. All participants volunteered for the study for monetary compensation. They signed an informed consent form prior to participation. After completing the study, they were debriefed and paid for their participation.

We collected as much data as possible, given the research funding constraints. A statistical power analysis was conducted using G*Power v3.1.9.2 (Faul, Erdfelder, Lang, & Buchner, **2007**). We assumed that the effect size of this study would be equivalent to that observed in our previous study (Matsunaga et al., **2017**). A priori power analysis estimated the necessary sample size for this study as N = 158 (analysis of covariance [ANCOVA]: fixed effects, main effects, and interactions, F-tests; effect size = .25; alpha error = .05; 1-beta error = .8; numerator df = 2, number of groups = 6, number of covariates = 3). We set a target sample size of approximately 200 based on a predicted dropout rate of 20%.

Genotype Analysis

Genomic DNA was extracted from nail samples of the participants using ISOHAIR kits (Nippon Gene, Tokyo, Japan). The SNP marker for rs6311 was genotyped using the commercially available TaqMan SNP Genotyping Assay (Thermo Fisher Scientific, Waltham, MA, USA) containing gene-specific polymerase chain-reaction (PCR) primers and two allele-specific probes conjugated with either VIC or FAM fluorescent tags. Each PCR mixture consisted of DNA

templates, the SNP-specific genotyping assay, and TaqMan genotype master mix (Thermo Fisher Scientific). All PCR and allelic discrimination reactions were performed on the StepOne Plus Real-Time PCR System (Thermo Fisher Scientific). The genotype distribution for the *HTR2A* variants consisted of 39 AA, 101 GA, and 53 GG in the Japanese cohort and 31 AA, 103 GA, and 56 GG in the American cohort; 24 samples were missing. The *HTR2A* genotype distribution was similar to that reported in a previous study (Dressler, Balieiro, Ribeiro, & Dos Santos, **2009**) and resulted in Hardy–Weinberg equilibrium, χ^2 (2) = 1.9 and 4.8, p = .39 and .09 for the Japanese and American cohorts, respectively.

Evaluation of Social Sharing of Happiness

Participants completed the questionnaire in a laboratory setting. Before answering the questions, participants were asked to think of a same-sex friend and rate the closeness between themselves and the friend using the Inclusion of Other in Self (IOS) Scale (Woosnam, **2010**). Using a vignette-based questionnaire, the participants were then asked to evaluate their level of happiness in the presence (and absence) of the imagined friend experiencing a positive-valence life event while they themselves were in an emotionally neutral life event. We selected two cases related to human relationships (friendship and romantic relationship) based on the previous emotional event imagination task, which was shown to induce happy feelings (Matsunaga et al., **2017**). Participants imagined experiencing each event alone (absence) and with a happy friend (presence). Therefore, a 2 (case) × 2 (presence/absence) situation was used. The participants were asked to evaluate their happy feelings on a 7-point Likert scale (1 = *extremely unhappy*, 2 = *very unhappy*, 3 = *a little unhappy*, 4 = *neither*, 5 = *a little happy*, 6 = *very happy*, and 7 = *extremely happy*) while imagining the following four situations: “Your friendship has not changed (your friend is irrelevant to this event)” (friendship, absence condition); “Your friendship has not changed, but your friend has made new and reliable friends, and has deepened their ties with them recently” (friendship, presence condition); “Your romantic relationship has not changed (your friend is irrelevant to this event)” (romantic relationship, absence condition); and “Your romantic relationship has not changed, but your friend has become closer with the romantic partner recently” (romantic relationship, presence condition). All four situations are shown on the same paper, so it was not possible to counterbalance the order in this study.

Evaluation of Subjective Happiness Level

Global well-being was assessed using the Subjective Happiness Scale (SHS; Lyubomirsky & Lepper, **1999**; Shimai, Otake, Utsuki, Ikemi, & Lyubomirsky, **2004**), which exhibits excellent psychometric properties, such as high internal consistency, a unitary structure, and stability over

time (Lyubomirsky & Lepper, **1999**), and is therefore widely used for evaluating subjective happiness levels (Matsunaga et al., **2016**, **2018**). Along with assessing whether a person is happy or unhappy, the SHS assesses their positive personal traits. The scale comprises four items, with each item answered on a 7-point Likert scale. Participants were asked to circle the point on the scale that they felt described them the most accurately regarding the following items: (a) "In general, I consider myself…" 1 (*not a very happy person*) to 7 (*a very happy person*); (b) "Compared to most of my peers, I consider myself…" 1 (*less happy*) to 7 (*more happy*); (c) "Some people are generally very happy. They enjoy life regardless of what is going on, getting the most out of everything. To what extent does this characterization describe you?" 1 *(not at all*) to 7 (*a great deal*); and (d) "Some people are generally not very happy. Although they are not depressed, they never seem as happy as they might be. To what extent does this characterization describe you?" 1 (*not at all*) to 7 (*a great deal*). The internal consistency, test–retest reliability, and convergent discriminant validity of the SHS have been previously confirmed (Lyubomirsky & Lepper, **1999**; Shimai et al., **2004**). Cronbach's alpha scores for the SHS were .84 and .88 in the Japanese and American samples, respectively.

Statistical Analysis of the Questionnaire Results

For the vignette-based questionnaire, we first calculated the mean score of the two cases in the absence and presence conditions, and compared the raw rating scores in the Japanese (n = 193) and American (n = 190) samples between *HTR2A*genotypes using 2 (country: Japan and United States) × 2 (condition: absence and presence) × 3 (*HTR2A* genotypes) repeated-measures analysis of variance (rmANOVA) followed by Bonferroni-corrected multiple comparisons. Then, to assess the effect of *HTR2A* on social sharing of happiness, we subtracted the score of the absence condition from that of the presence condition, calculated the mean score of the two cases, and compared the subtracted rating scores in the Japanese and American cohorts between *HTR2A* genotypes using ANCOVA with three covariates (age, gender, and closeness [IOS Scale]) followed by Bonferroni-corrected multiple comparisons. For the SHS, we compared the SHS scores in the Japanese and American samples using 3 (*HTR2A* genotypes) × 2 (country) ANCOVA with two covariates (age and gender) followed by Bonferroni-corrected multiple comparisons. The mean rating score in the vignette-based questionnaire, SHS, and IOS Scale were also compared between the Japanese and American participants using Student's t-test.

Results

Table **1** shows the descriptive statistics of the variables (raw rating score in the absence/presence conditions, subtracted rating score, SHS, and IOS Scale) for both cultural groups. Statistical

analyses indicated that both raw rating scores in the absence ($p = .002$) and presence ($p < .001$) conditions were higher in the American cohort than for the Japanese participants. However, the subtracted rating score, which was interpreted as the social sharing of happiness, tended to be higher in the American cohort than for the Japanese participants ($p = .09$). No significant difference was observed in the subtracted rating score, SHS, and IOS Scale values.

Table 1. Descriptive statistics of variables by cultural group

Variable	Japan	United States	Cultural difference (*p*-value)
Rating score in absence condition	4.42 ± 0.63	4.67 ± 1.00	.002
Rating score in presence condition	4.60 ± 0.94	4.99 ± 1.03	<.001
Subtracted rating score	0.18 ± 0.80	0.33 ± 0.88	.09
SHS	4.74 ± 1.07	4.76 ± 1.29	.90
IOS Scale	3.99 ± 1.45	3.81 ± 1.62	.26

- *Note*. Results are expressed as means ± standard deviation. Variables were compared using Student's *t*-test. Subtracted rating score indicates the mean score of the subtracted rating score of the absence condition from that of the presence condition in the vignette-based questionnaire, which is interpreted as the "social sharing of happiness." SHS = Subjective Happiness Scale; IOS Scale = Inclusion of Other in Self Scale.

Table 2 shows the raw rating scores in the absence and presence conditions between individuals with different *HTR2A* genotypes among the Japanese and American cohorts. A three-factor (country, condition, and *HTR2A*) rmANOVA revealed significant main effects of country (F [1, 377] = 10.95, $p = .001$, $\eta_p^2 = .03$) and condition (F [1, 377] = 18.44, $p < .001$,  = .05). The rmANOVA also revealed significant interaction between the condition and *HTR2A* genotype

(F [2, 377] = 3.16, p = .043,  = .02). Multiple comparisons tests indicated that the raw rating scores in the absence and presence conditions were significantly different in individuals harboring the GG ($p < .001$) and AG ($p < .001$) genotypes but were not statistically significant in the AA group (p = .89).

Table 2. Raw rating scores for each *HTR2A* genotype in the questionnaire

	Japan			United States		
Condition	**GG**	**GA**	**AA**	**GG**	**GA**	**AA**
Absence	4.45 (0.69)	4.37 (0.56)	4.51 (0.73)	4.75 (0.88)	4.59 (1.01)	4.82 (1.17)
Presence	4.73 (0.99)	4.54 (0.89)	4.59 (1.08)	5.10 (0.99)	4.99 (0.99)	4.77 (1.22)

- *Note*. Results are expressed as means (standard deviation). Variables were compared using 2 (country) × 2 (situation) × 3 (*HTR2A* genotypes) repeated-measures ANOVA followed by Bonferroni-corrected multiple comparisons.

To examine the effect of genetics and culture interaction in the social sharing of happiness, we then compared the subtracted rating scores that were interpreted as the social sharing of happiness, as mentioned above. Figure **1** shows the mean subtracted rating scores between individuals with different *HTR2A* genotypes in the Japanese and American cohorts. A two-factor (*HTR2A* and country) ANCOVA revealed a significant main effect of *HTR2A* on the rating score (F [2, 367] = 3.31, p = .038,  = .02). A multiple comparisons test also indicated that the subtracted happiness rating score in the AA genotype group was significantly lower than in the AG group (p = .049). The score in the AA genotype group also tended to be lower than in the GG group (p = .067). No significant interaction was observed between *HTR2A* and country in the mean subtracted rating scores (F (1, 373) = 0.33, p = .56).

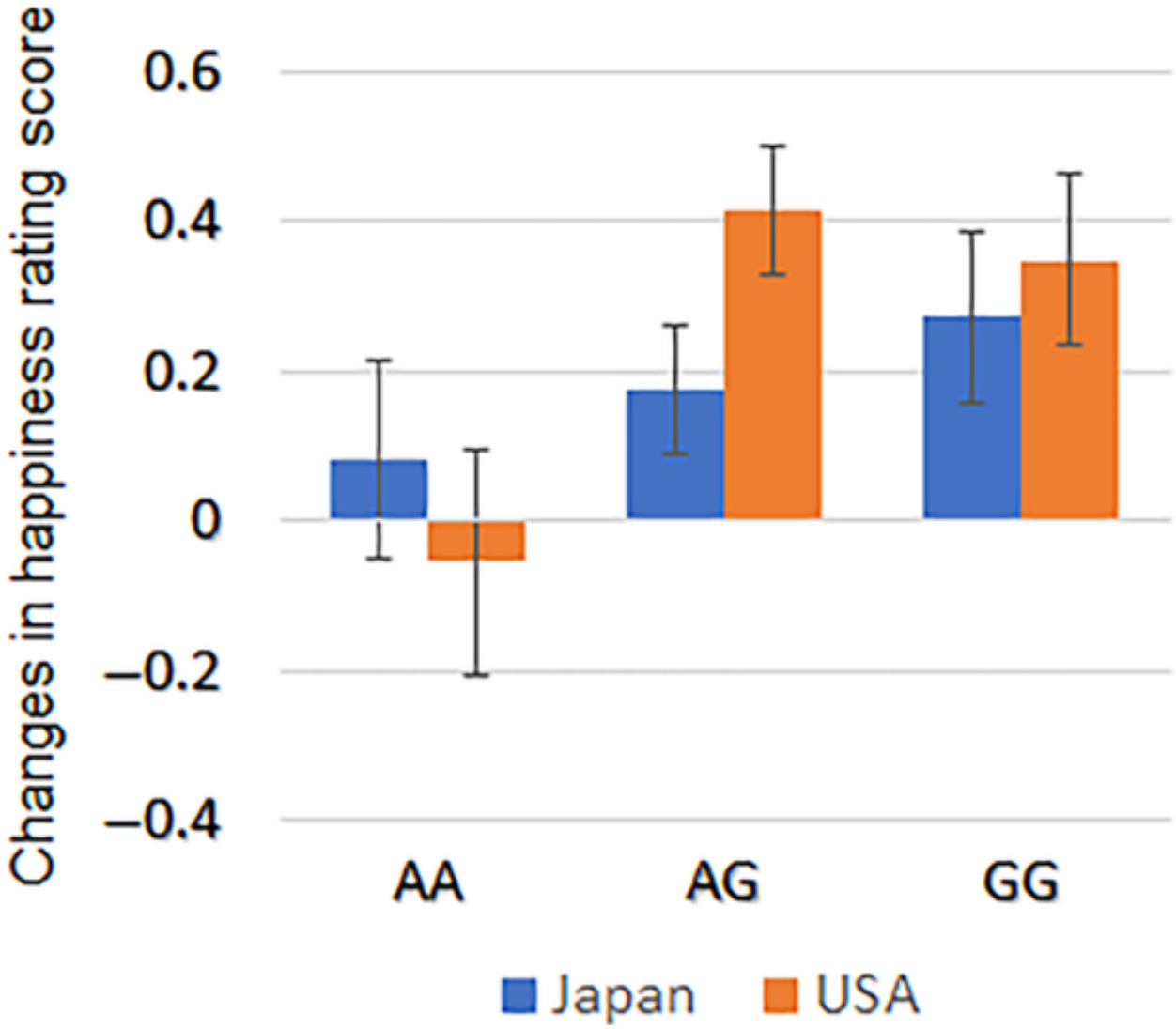

Figure 1

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Associations between *HTR2A* polymorphism and happiness-related empathy. The bar graph indicates the mean difference (between presence and absence of an imagined friend experiencing a positive-valence life event) in their happiness rating score on a vignette-based questionnaire (original evaluation score range: 1–7), interpreted as the social sharing of happiness, in relation to culture (Japan, USA) and *HTR2A* genotype (AA, AG, GG). Error bars represent the mean ± standard error of the mean of the rating score. A, adenine; G, guanine.

Additionally, we examined the effect of genetic and culture interaction on global happiness. The SHS scores among *HTR2A* genotypes were AA: 4.77 ± 0.19 (mean ± standard error of the mean), AG: 4.84 ± 0.12, and GG: 4.79 ± 0.16 for the Japanese cohort, and AA: 4.62 ± 0.21, AG: 4.78 ± 0.12, and GG: 4.56 ± 0.16 for the American cohort. A 3 (*HTR2A* genotypes) × 2 (country) ANCOVA with 2 covariates (age and gender) indicated no significant main effect

of *HTR2A* (F [2, 373] = 0.53, p = .59) and no significant interaction between *HTR2A* and country (F [2, 373] = 0.18, p = .84).

Considering that the evaluative happiness differed with age, and the sample size in this study was relatively small, we performed a supplemental analysis. We conducted a two-factor (*HTR2A* AA vs. AG + GG and country) ANCOVA using a larger sample cohort (n = 723). We compared the SHS scores of the first Japanese student cohort (n = 193), an additional Japanese student cohort (n = 409), and the American cohort (n = 121) of participants under 30 years of age, in accordance with their *HTR2A* genotypes (*see* Supplemental Methods in the Supporting Information). As shown in **Figure S1**, the ANCOVA revealed a significant main effect of *HTR2A* on the SHS score (F [1, 717] = 4.67, p = .031,  = .01), and a multiple comparisons test indicated that the SHS score in the AA genotype group was significantly lower than that of the G carriers (p = .031). No significant interaction between *HTR2A* and country was observed in the SHS score (F [1, 717] = 0.77, p = .38).

Discussion

Previous studies have indicated that the effect of gene polymorphisms on emotional processing is influenced by culture, as certain genotypes are manifested in different forms, depending on inputs from the social environment (H. S. Kim, Sherman, Taylor, et al., **2010**; Matsunaga et al., **2018**). The results of the present study suggest that the effect of *HTR2A* on the rating scores of happiness may not differ among cultures, with *HTR2A* rs6311 G carriers feeling happier in the presence of a happy friend than those harboring the AA genotype.

There is consensus that Western cultures are individualistic while Eastern cultures are collectivistic (Hofstede, **1980**; but see also Oyserman, Coon, & Kemmelmeier, **2002**). Previous studies have indicated that people in collectivistic countries are more prone to emotional contagion than are people in individualistic countries (Hatfield, Bensman, Thornton, & Rapson, **2014**; Markus & Kitayama, **1991**). People in collectivistic cultures often experience other-focused positive emotions, such as feelings of connection or familiarity with another person; however, these other-focused positive emotions are experienced negatively among independent selves (such as timid individuals; Hatfield et al., **2014**; Markus & Kitayama, **1991**). Furthermore, the definition of happiness is known to vary by country/culture (Oishi, Graham, Kesebir, & Galinha, **2013**). The concept of happiness in Western cultures, such as the United States and Canada, centers on positive inner feelings including pleasure and joy (Oishi et al., **2013**). In contrast, in Eastern cultures, such as Japan, happiness is based on the fortune of

external circumstances (Oishi et al., **2013**; Oyama, **2012**). In fact, a previous study indicated that Americans associated the positive hedonic experience of happiness with personal achievement, whereas Japanese associated it with social harmony (Uchida & Kitayama, **2009**). Thus, it is possible that the effect of *HTR2A* on social sharing of happiness is more prominent in Japanese people than in Americans. However, our present findings revealed that there was no cultural difference in the effect of social sharing of happiness between Japanese and American participants. It is thus possible that there may not be significant cultural differences in positive emotional contagion, which is in accordance with a previous study (Kuang et al., **2019**).

The effect of an interaction between a polymorphism in the human cannabinoid receptor and culture on happiness processing has been observed (Matsunaga et al., **2018**). Specifically, the effect of a cytosine (C) to thymine (T) change in the human cannabinoid receptor 1 (*CNR1*) gene (rs806377), which is associated with sensitivity to external positive emotional stimuli, on the perception of happiness was found to differ between Western (Canadian) and Eastern (Japanese) populations. *CNR1* C-allele carriers, who may be sensitive to positive social relationships, reported a relatively higher degree of happiness among the Japanese cohort, whereas in the Canadian group, individuals with the TT genotype had a higher level of subjective happiness compared with that of C carriers. People amidst happy circumstances and opportunities, including happy people, may be happier in the context of Japanese culture. In contrast, in North American cultures, people who are not influenced by the well-being of others may be happier. Thus, it is possible that serotonin and endocannabinoids may influence happiness through different underlying molecular mechanisms in different cultures.

A study examining cultural differences in social norms regarding emotional support seeking demonstrated that while American norms favor it, Korean norms discourage it (H. S. Kim, Sherman, & Taylor, **2008**). According to a study of oxytocin, a gene associated with empathy, individuals harboring the G allele of the oxytocin receptor (*OXTR*) polymorphism rs53576, known to be associated with socio-emotional sensitivity, showed more enhanced emotional support seeking in distress conditions than individuals with the AA genotype in Western cultures (United States), whereas individuals in Eastern cultures (Korea) did not show differences between genotypes (H. S. Kim, Sherman, Sasaki, et al., **2010**). Although we only investigated the effect of a single *HTR2A* polymorphism on the social sharing of happiness, additional investigations of the genetic-culture interactions of *HTR2A* on social support may provide valuable information.

Global and experiential well-being have been indicated to partially overlap (Otake et al., **2006**; Schimmack, **2008**; Seligman et al., **2005**). For example, previous total time spent with a romantic

partner elevates episodic and global positive effects, whereas the company of a friend only influences episodic positive effects (Hudson et al., **2020**). Based on these findings, we predicted that G-allele carriers of *HTR2A* may experience higher global well-being than those with the AA genotype, as G-allele carriers can experience greater happiness when their friends experience happy events. However, the present results showed no significant main effect of *HTR2A* and no significant interaction between *HTR2A* and country on the SHS. Considering that subjective happiness level varies depending on age (Blanchflower & Oswald, **2009**; Frijters & Beatton, **2012**) and that a small sample size can be statistically unstable (Culverhouse et al., **2018**), we performed a supplemental analysis, (as described in the Supplemental Methods and Supplemental References). The SHS score of the AA genotype group was found to be significantly lower than that of G carriers, suggesting that *HTR2A* not only influences experiential well-being through empathizing with friends but also partially influences global well-being.

Although the underlying mechanisms by which the SNP rs6311 in *HTR2A*influences social sharing of happiness has not been clarified, recent findings have offered suggestions. Damasio, Tranel, and Damasio (**1991**) previously proposed the somatic marker hypothesis, where physical emotional responses, such as rapid heartbeat, evoked by external emotional stimuli guide behavioral responses, particularly decision-making. Porges (**2009**) also established the polyvagal theory, which behaviorally links the mammalian myelinated vagal neurons, which originate in the nucleus ambiguus, to social communication (such as facial expression, vocalization, or listening). Moreover, recent studies have shown that the parasympathetic nervous system is associated with empathy; for instance, an association between resting parasympathetic dysfunction and prosocial helping deficits (Sturm et al., **2018**) as well as increased parasympathetic response during self-compassion training (J. J. Kim et al., **2020**) have been reported. Previous studies have demonstrated that a 5-HT2A agonist, m-CPP (1-[3-chlorophenyl] piperazine dihydrochloride), inhibits vagally induced bradycardia (Morán, Velasco, Martín, & San Román, **1994**), whereas the 5-HT2A antagonist, ketanserin, facilitates excitatory neurotransmission to cardiac vagal neurons (Gorini, Jameson, & Mendelowitz, **2009**). Thus, 5-HT2A receptor-dependent systems can modulate vagal tones, and it is suggested that the parasympathetic nervous responses during social sharing of happiness may differ between *HTR2A*G carriers and the AA genotype, which is considered to be associated with increased expression of 5-HT2A receptors (Parsons, D'Souza, Arranz, Kerwin, & Makoff, **2004**). Such differences in vagal tone may influence the self-evaluation process in social sharing of happiness. In the present study, the data did not allow us to determine whether parasympathetic activity was associated with the effects of *HTR2A* polymorphism on the social sharing of

happiness. Thus, a future replication study considering such parasympathetic vagal activities will serve to clarify our findings.

Our study has several limitations. First, previous studies have indicated the culture–sex interaction and gene–sex interaction in empathy (Nishina, Takagishi, Inoue-Murayama, Takahashi, & Yamagishi, **2015**; Zhao et al., **2019**), which suggests that culture, sex, and genetics interact and influence both psychological and physical characteristics (Schmitt, **2015**). Thus, it is possible that interactions among culture, sex, and *HTR2A* polymorphism may alter the social sharing of happiness. Second, although the present study indicated that there was no difference in the effect of *HTR2A* on self-reported social sharing of happiness between Japanese and American participants, it is possible that differing effects can be induced by an emotion evocation task that elicits stronger emotional reactions compared with a questionnaire. Although our previous study demonstrated that G carriers of *HTR2A* felt happier in the presence of their happy friends compared with individuals harboring the AA genotype in both the fMRI and questionnaire-based experiments (Matsunaga et al., **2017**), future studies using emotion evocation tasks may be needed to clarify this issue. Third, since the purpose of this study was to examine the effects of *HTR2A* in American participants, we did not specifically consider comparability between the two samples (the Japanese participants were undergraduate students, whereas the American participants were residents of the Chicago area). Thus, several confounding factors, such as meaning systems, education style, labor market, and legal systems, may exist. In the case of the present study, the socioeconomic status (SES) of the countries may also represent a confounding variable. As the American sample was more diverse than the Japanese sample, participants with relatively low SES (such as those without a college degree) may be more prevalent in the American cohort. A previous study reported that lower-class individuals are higher in empathic accuracy than are upper-class individuals (Kraus, Côté, & Keltner, **2010**). As for cultural differences in empathy, another study reported that people in collectivistic societies likely show high empathic concern (Chopik, O'Brien, & Konrath, **2017**). When combining these findings, an alternative explanation of the current study data is that the absence of cultural differences may be an artifact due to a relatively high proportion of lower-class individuals in the American cohort than in the Japanese cohort. Thus, an additional study using comparable samples, including SES data, may be necessary. Nevertheless, the present findings indicate an association between *HTR2A* polymorphisms and social sharing of happiness in both Western and Eastern cultures. Hence, our findings can be used to develop strategies to increase the degree of happiness tailored to specific countries or cultures, which would represent a major contribution to the field of social psychology.

Conflict of Interest

The authors declare there are no conflicts of interest associated with this manuscript.