Independent self-construal mediates the association between CYP19A1 gene variant and subjective well-being

Xing Yang\textsuperscript{a,b}, Yafang Yang\textsuperscript{a}, Mengying Xue\textsuperscript{a}, Pengpeng Fang\textsuperscript{c}, Guomin Shen\textsuperscript{e}, Kejin Zhang\textsuperscript{c,d}, Xiaocai Gao\textsuperscript{c,d}, Rongjun Yu\textsuperscript{c,f}, Pingyuan Gong\textsuperscript{a,b,c,d,*}

\textsuperscript{a} Shaanxi Key Laboratory for Animal Conservation, Northwest University, Xi’an 710069, China
\textsuperscript{b} Key Laboratory of Resource Biology and Biotechnology in Western China, Ministry of Education, Northwest University, Xi’an 710069, China
\textsuperscript{c} College of Life Science, Northwest University, Xi’an 710069, China
\textsuperscript{d} Institute of Population and Health, Northwest University, Xi’an 710069, China
\textsuperscript{e} Laboratory of Medical Molecular Biology, Henan University of Science and Technology, Luoyang 471003, China
\textsuperscript{f} Department of Psychology, National University of Singapore, 117570, Singapore

**ARTICLE INFO**

**Keywords:**
- Self-construal
- Subjective well-being
- Aromatase
- Testosterone
- Estrogen

**ABSTRACT**

Testosterone and estrogen are involved in self-related behavioral dispositions and experiences of subjective well-being. In this study, we investigated to what extent the aromatase (CYP19A1) gene, which encodes an enzyme in converting testosterone into estrogen, contributes to subjective well-being and in another self-related disposition: independent and interdependent self-construal. In study 1, a meta-analysis showed that the GG genotype of CYP19A1 (a G/A substitution at Val80, rs700518) was associated with higher testosterone and lower estradiol. In study 2, an empirical study of individuals with the GG (n = 115), AG (n = 286) and AA (n = 193) genotypes indicated that individuals with the GG genotype exhibited higher independent self-construal and higher subjective well-being. The association between the GG genotype of CYP19A1 Val80 and subjective well-being was mediated by the independent self-construal. Our findings reinforce the idea that personality traits such as independent self-construal explain the link between genetic variant and subjective well-being.

1. Introduction

The answer to the question “Who am I?” embodies how individuals make meaning of themselves (Cross, Hardin, & Gereck-Swing, 2011), sometimes called self-construal. Self-construal consists of two dimensions: independent self-construal and interdependent self-construal (Markus & Kitayama, 1991). The independent dimension reflects a person’s emphasis on thoughts, feelings, uniqueness, and self-expression, whereas the interdependent dimension reflects a person’s emphasis on the external and public features of the self, such as status and relationships (Singelis, 1994). For example, individuals with an independent construal tend to view happiness as related to the themes of personal achievement, emotional expression, and mutual confirmation of inner positive attributes (Uchida, Norasakkunkit, & Kitayama, 2004).

Self-construal is a powerful regulator of individual differences in self-related behavioral dispositions of important social behaviors (Markus & Kitayama, 1991; Sui & Han, 2007) and of how people manage their relationships, such as coping with interpersonal closeness and improving relationship quality (Holland, Roeder, van Baaren, Brandt, & Hannover, 2004; Morry & Kito, 2009). Individuals with higher independent self-construal tend to exhibit higher social dominance (Kupper & Zick, 2011). They also perceive aggression...
as a means to reestablish their positions, whereas individuals with an interdependent self-construal perceive aggression as a failure in controlling their emotions and desires (Cross & Madson, 1997).

Several lines of evidence suggest that the link between self-construal and self-related behavioral dispositions may be related to levels of testosterone and estrogen. The contribution of self-construal to aggressive behavior has been shown to be regulated by testosterone levels (Welker et al., 2016). An acute increase in testosterone levels is positively associated with aggressive behavior for individuals with an independent self-construal, whereas basal testosterone levels are negatively associated with aggression for individuals with an interdependent self-construal (Welker et al., 2016). Testosterone, produced in the testis and adrenal glands, functions as an androgen with respect to its physiological effects on social behaviors such as social dominance (Sellers, Mehl, & Josephs, 2007; Van Bokhoven et al., 2006), competition (van der Meij, Almela, Buunk, Fawcett, & Salvador, 2012), and aggression (Crespi, 2016). Individuals with higher levels of salivary testosterone show overt social dominance (Sellers et al., 2007), competition (van der Meij et al., 2012), proactive aggression (Van Bokhoven et al., 2006), and an independent style of talking (Dabbs, Bernieri, Strong, Campo, & Milun, 2001). While testosterone is the primary male sex hormone, the enzymatic products of testosterone, estrogen, is the primary female sex hormone. Studies have found that estrogen not only contributes to dominance status, social recognition, territorial aggression, and mate choice in animals (Davies et al., 2016; Ervin et al., 2015; Filby, Paull, Searle, Ortiz-Zarragoitia, & Tyler, 2012), but also is involved in emotional responses (Olsson, Kopsida, Sorjonen, & Savic, 2016) and decision making in competitive bidding in humans (Chen, Katuscak, & Ozdenoren, 2013).

It has been found that testosterone and estrogen are also closely linked with individuals’ subjective well-being (Davis & Tran, 2001; McDuff & Beange, 2003; Nathanor-Böös, Flöter, Jarkander-Rolf, Carlström, & Von Schoultz, 2006). Subjective well-being, a complex psychological construct, refers to the positive cognitive and affective evaluation of one’s life (Diener, Suh, Lucas, & Smith, 1999) and the psychological experiences of self-realization and positive social relationships (Ryan & Deci, 2001). Transdermal testosterone replacement improves menopausal women’s psychological well-being, with the greatest changes in depressed mood, sexual enjoyment and satisfaction with orgasms (Davis & Tran, 2001; Nathanor-Böös et al., 2006), and women receiving estrogen replacement feel less anxiety and depression and more general well-being (Aziz, Brannstrom, Bergquist, & Silfverstolpe, 2005; Kotz, Alexander, & Dennerstein, 2006; Nathanor-Böös, von, & Carlström, 1993).

The above evidence points out that both self-construal and subjective well-being are connected with testosterone and estrogen levels, suggesting that they may share a similar biophysical basis. Studies have also found that self-construal influences individuals’ actions, ideas, and feelings (Sun & Yu, 2014) as well as the experiences of well-being and the pursuit of happiness (Duncan, Ormaghi, & Graziani, 2013; Suh, Diener, & Updegraff, 2008). Given the critical role of self-construal in subjective well-being and its link to testosterone and estrogen levels, it is reasonable to speculate that self-construal may play a role in hormone levels’ contribution to subjective well-being.

The CYP19A1 gene has been studied as an indicator of levels of testosterone and estrogen. This gene provides instructions for making an enzyme called aromatase. Aromatase is a rate-limiting enzyme that converts male sex hormone androgens (e.g., testosterone) to different forms of the female sex hormone estrogen (Gruber, Tschugguel, Schneeberger, & Huber, 2002). Aromatase also regulates the ratio of testosterone to estrogen in the brain (Aversa et al., 2016; Wu et al., 2017), which is related to maternal aggression (Unger et al., 2015) and aggressive communication with partners (Akther et al., 2015). The CYP19A1 gene regulates the processes of androgen degradation and estrogen biosynthesis (Lorentzon, Swanson, Eriksson, Mellstrom, & Ohlsson, 2006; Peter et al., 2008; Sommer et al., 2004; Yeap et al., 2016) and is associated with aromatase deficiency (Belgorosky, Guercio, Pepe, Saraco, & Rivarola, 2009) and aromatase excess syndrome (Fukami et al., 2011). The CYP19A1 Val80 (rs700518) polymorphism, G/A at Val80 in exon 3 of the CYP19A1 gene, has been shown to underpin the variance of aromatase activity.

Several studies have investigated the impacts of this polymorphism on levels of testosterone and estrogen (Lorentzon et al., 2006; Peter et al., 2008; Sommer et al., 2004; Yeap et al., 2016). However, these studies produced inconsistent results regarding the relationship between this polymorphism and the levels of testosterone/estrogen. As for the levels of testosterone, Peter’s study indicated that the GG genotype, as compared with AA genotype, was related to higher levels of testosterone in males (Peter et al., 2008), while Sommer’s study showed that the GG genotype was related to lower levels of testosterone in females (Sommer et al., 2004). Meanwhile, Lorentzon’s and Yeap’s studies failed to detect the relationship in males at all (Lorentzon et al., 2006; Yeap et al., 2016). As for the levels of estrogen, Peter’s study indicated that the GG genotype was related to lower levels of estrogen both in males and females (Peter et al., 2008), while Somner’s study showed that the GG genotype was related to higher levels of estrogen in females (Sommer et al., 2004). Moreover, Lorentzon’s study did not detect any significant difference in the levels of estrogen between the GG genotype group and AA genotype group (Lorentzon et al., 2006). The link between CYP19A1 Val80 and levels of testosterone and estrogen is yet to be established.

We conducted two studies to examine links between hormone levels, self-construal, and subjective well-being. In Study 1 we conducted a statistical meta-analysis to examine the relationship between CYP19A1 Val80 polymorphism and levels of testosterone and estrogen. In Study 2 we examined a sample of individuals who varied on the CYP19A1 Val80 polymorphism to test the links between the CYP19A1 gene and individual differences in self-construal, subjective well-being and its three aspects (i.e., cognitive, affective and psychological subjective well-being). Given that women have been shown to have higher interdependent self-construal than men (Kashiya et al., 1995; Watkins et al., 2003), gender was taken into account in these analyses. Moreover, to address the genetic contribution, we also examine the effect of CYP19A1 Val80 after controlling for contributions of environmental variables (e.g., household income, life stress, life hopes, and religious beliefs). Finally, as previous studies demonstrating the link of self-construal with subjective well-being (Dabbs et al., 2001; Kwan, Bond, & Singelis, 1997; Yu, Zhou, Fan, Yu, & Peng, 2014), we are interested in examining the extent to which self-construal mediates the association between the CYP19A1 gene and subjective well-being.
2. Study 1, Meta-analysis on CYP19A1 Val80 and levels of testosterone and estrogen

2.1. Identification and eligibility of relevant studies

Relevant studies were identified in a search of English-language articles published before March 31, 2017. Two researchers independently screened, identified for inclusion, and determined the eligibility of the studies by using the search terms “CYP19A1 Val80” or “rs700518” and “testosterone level” or “estradiol level” in the ISI Web of Science and PubMed databases. The selected studies met the following criteria: (a) used an experimental design to evaluate the association between CYP19A1 Val80 and the levels of testosterone/estrogen in humans; (b) contained information necessary to calculate effect sizes.

After reaching a consensus, six primary studies including six independent samples were selected (Lorentzon et al., 2006; Napoli et al., 2015, 2013; Peter et al., 2008; Somner et al., 2004; Yeap et al., 2016) for possible inclusion in the meta-analysis. However, Napoli’s samples (2013, 2015) were excluded given that some participants in the studies used aromatase inhibitor, a substance that influences the activity of aromatase. Finally, the results of the other four primary studies were pooled in the meta-analysis.

2.2. Results

The meta-analysis revealed that the CYP19A1 Val80 polymorphism was significantly associated with individual differences in testosterone levels (Fig. S1 in Supplementary Materials 1). Individuals with the GG genotype had higher levels of testosterone than the AA genotype group, with $Z = 7.999, p < 0.001$, effect size = 0.491 for the fixed effects model, and $Z = 0.545, p = 0.586$, effect size = 0.034 for the random effects model. Individuals with the GG genotype also had higher levels of testosterone than the AG genotype group, with $Z = 6.026, p < 0.001$, effect size = 0.337 for the fixed effects model, and $Z = 0.105, p = 0.916$, effect size = 0.006 for the random effects model, and the AA genotype group had lower levels of testosterone than the AG genotype group, with $Z = -4.809, p < 0.001$, effect size = $-0.252$ for the fixed effects model, and $Z = -1.318, p = 0.188$, effect size = 0.069 for the random effects model.

The meta-analysis also revealed that the CYP19A1 Val80 polymorphism was significantly associated with individual difference in estradiol levels (Fig. S2 in Supplementary Materials 1). Individuals with the GG genotype had lower levels of estradiol than those with the AA genotype group, with $Z = -7.736, p < 0.001$, effect size = $-0.456$ for the fixed effects model, and $Z = -2.099, p = 0.036$, effect size = $-0.124$ for the random effects model. Moreover, individuals with the GG genotype had lower levels of estradiol than the AG genotype group, with $Z = -9.796, p < 0.001$, effect size = $-0.493$ for the fixed effects model, and $Z = -1.369, p = 0.171$, effect size = $-0.069$ for the random effects model, and the AA genotype group had higher levels of estradiol than the AG genotype group, with $Z = 7.478, p < 0.001$, effect size = 0.389 for the fixed effects model, and $Z = 1.504, p = 0.133$, effect size = 0.078 for the random effects model.

3. Study 2: Materials and methods

3.1. Participants

Five hundred and ninety-four second-year college students (68.9% female, mean age = 20.0, SD = 1.4) were recruited from twenty classes at Henan University of Science and Technology, China. The power analysis indicated that a sample of 488 is required (two-tailed $\alpha = 0.05, 1-\beta = 0.80$) to detect a minimum regression coefficient representing the impact of CYP19A1 on self-construal and subjective well-being of 0.141 (i.e., the coefficient of determination $R^2 > 2.0\%$). The sample size ($N = 594$) of this study demonstrated 96.58% power in detecting significant associations (two-tailed $\alpha = 0.05$, effect size = 0.141). The participants were in the normal range of mental health as indicated by an average global severity index of $M = 0.763 (SD = 0.551)$ on the Chinese version (Huang, 2009) of the Symptom Checklist-90 (Derogatis, Lipman, & Covi, 1973); this index is the average score of all 90 items and reflects overall psychological distress, Supplementary Materials 2. Written informed consent was obtained from each participant and the research was conducted in accordance with the Declaration of Helsinki. This study was approved by the Ethics Committee of the College of Life Science, Northwest University, China.

3.2. Self-construal assessment

The two dimensions of self-construal (independent and interdependent) were measured by the self-reported Chinese version (Wang, Yuan, & Xu, 2008) of the Self-Construal Scale (SCS) (Singelis, 1994). This scale consists of a 12-item independent self-construal subscale and a 12-item interdependent self-construal subscale. The independent self-construal subscale taps one’s sense of independence and uniqueness, and one’s internal repertoire of thoughts and feelings (e.g., “I enjoy being unique and different from others in many respects”). The interdependent subscale measures beliefs about relationships between self and others and the degree to which individuals see themselves as connected with others (e.g., “It is important for me to maintain harmony within my group”). The responses were scored on a 7-point Likert scale, ranging from 1 (strongly disagree) to 7 (strongly agree). The scoring procedure followed Singelis’s (1994) suggestions. In the current sample, the two subscales were significantly correlated with each other, $r = 0.553, p < 0.001$. The Cronbach’s alphas were 0.692, and 0.777 for the independent subscale and interdependent subscale, respectively, values that were similar to those reported by Wang (independent subscale: $\alpha = 0.81$; interdependent subscale: $\alpha = 0.76$; 2008) and Singelis (independent subscale: $\alpha = 0.69–0.70$; interdependent subscale: $\alpha = 0.73–0.74$; 1994).
Scoring procedure followed Diener (2010). The Cronbach’s αs are presented in Table 1. A general subjective well-being score was then calculated as the mean of the standardized scores on the Scale of Positive and Negative Experience (SPANE) (Diener et al., 2010). Therefore, information about socio-experiences associated with positive relationships and a positive sense of the meaning of life (e.g., “I lead a purposeful and meaningful life”). The responses were scored on a 7-point Likert scale, ranging from 1 = “strongly disagree” to 7 = “strongly agree.” The affective aspect was measured with a translated version of the Scale of Positive and Negative Experience (SPANE) (Diener et al., 2010). This scale includes 12 items, six about positive feelings (e.g., “joy”) and six about negative feelings (e.g., “sadness”). The participants indicated how often they showed these feelings in the past four weeks, with 1 indicating “seldom” and 5 indicating “very often.” The score on the SPANE, subtracting the negative feelings score from the positive feelings score, is the index of affective well-being. The psychological aspect was assessed with a translated version of the Flourishing Scale (FS) (Diener et al., 2010). This scale consists of 8 items used to evaluate positive psychological aspects of individuals’ subjective well-being (Dolan, Peasgood, & White, 2008; Røysamb, Tambs, Reichborn-Kjennerud, Neale, & Harris, 2003). This 5-item scale measures the extent to which participants are satisfied with their life. Participants rated their agreement with each statement (e.g., “in most ways my life is close to my ideal”) on a 7-point Likert scale, with 1 = “strongly disagree” and 7 = “strongly agree.” The affective aspect was measured with a translated version of the Scale of Positive and Negative Experience (SPANE) (Diener et al., 2010). This scale includes 12 items, six about positive feelings (e.g., “joy”) and six about negative feelings (e.g., “sadness”). The participants indicated how often they showed these feelings in the past four weeks, with 1 indicating “seldom” and 5 indicating “very often.” The score on the SPANE, subtracting the negative feelings score from the positive feelings score, is the index of affective well-being. The psychological aspect was assessed with a translated version of the Flourishing Scale (FS) (Diener et al., 2010). This scale consists of 8 items used to evaluate positive psychological experiences associated with positive relationships and a positive sense of the meaning of life (e.g., “I lead a purposeful and meaningful life”). The responses were scored on a 7-point Likert scale, ranging from 1 = “strongly disagree” to 7 = “strongly agree.” The scoring procedure followed Diener’s suggestion (2010). The Cronbach’s αs for the SWLS, SPANE and FS scores were displayed in Table 1. A general subjective well-being score was then calculated as the mean of the standardized Z scores on the SWLS, FS, and SPANE. The Cronbach’s α for this general subjective well-being score is also presented in Table 1.

### 3.3. Subjective well-being assessment

Three instruments were used to assess the cognitive, affective, and psychological aspects (Liu, Gong, Gao, & Zhou, 2017) of subjective well-being. The cognitive aspect was measured with the Chinese version (Xiong & Xu, 2009) of the Satisfaction with Life Scale (SWLS) (Diener, Emmons, Larsen, & Griffin, 1985). This 5-item scale measures the extent to which participants are satisfied with their life. Participants rated their agreement with each statement (e.g., “in most ways my life is close to my ideal”) on a 7-point Likert scale, with 1 = “strongly disagree” and 7 = “strongly agree.” The affective aspect was measured with a translated version of the Scale of Positive and Negative Experience (SPANE) (Diener et al., 2010). This scale includes 12 items, six about positive feelings (e.g., “joy”) and six about negative feelings (e.g., “sadness”). The participants indicated how often they showed these feelings in the past four weeks, with 1 indicating “seldom” and 5 indicating “very often.” The score on the SPANE, subtracting the negative feelings score from the positive feelings score, is the index of affective well-being. The psychological aspect was assessed with a translated version of the Flourishing Scale (FS) (Diener et al., 2010). This scale consists of 8 items used to evaluate positive psychological experiences associated with positive relationships and a positive sense of the meaning of life (e.g., “I lead a purposeful and meaningful life”). The responses were scored on a 7-point Likert scale, ranging from 1 = “strongly disagree” to 7 = “strongly agree.” The scoring procedure followed Diener’s suggestion (2010). The Cronbach’s αs for the SWLS, SPANE and FS scores were displayed in Table 1. A general subjective well-being score was then calculated as the mean of the standardized Z scores on the SWLS, FS, and SPANE. The Cronbach’s α for this general subjective well-being score is also presented in Table 1.

### 3.4. Environmental variables and personality traits

Previous studies have demonstrated that confounding factors influence individuals’ subjective well-being (Dolan, Peasgood, & White, 2008; Røysamb, Tambs, Reichborn-Kjennerud, Neale, & Harris, 2003). Therefore, information about socio-economic status (Haring, Stock, & Okun, 1984; Pinquart & Sörensen, 2000), number of siblings (Schnitzlein & Wunder, 2016), family type, caregivers, religious belief (Ellison, 1991; Witter, Stock, Okun, & Haring, 1985), life stress (McCullough, Huebner, & Laughlin, 2000; Seidlitz & Diener, 1993), life hopes (Demirli, Türkmén, & Arı, 2015), self-efficacy, self-consistency and congruence (Yu, Assor, & Liu, 2015; Yu, Zheng, Yan, & Wan, 2008), and mental health status (Suldo, Thalji, & Ferron, 2011; Wang, Jia, Zhu, & Chen, 2015) was collected. These factors were treated as potential confounding factors when investigating the effect of CYP19A1 Val80 on subjective well-being. A detailed description of these potential confounding factors is provided in the Supplemental materials 2.

### 3.5. Genotyping

For each participant, we collected 3–5 hairs with hair follicle cells and extracted genomic DNA from the cells using the Chelex-100 method (de Lamballerie, Chapel, Vignoli, & Zandotti, 1994). A 145 bp DNA fragment containing CYP19A1 Val80 was amplified by polymerase chain reaction (PCR), with the forward primer 5'-GGTGTGTTATGCTGACACCT-3' and the reverse primer 5'-AGACTCGCATGATTTCTCCTGA-3'. The G in the reverse primer was a mutation for introducing a restriction site for enzyme Rsa I in the PCR product. The PCR reaction system contained 2.50 μL 2 × reaction MIX (Golden Easy PCR System, TIANGEN), 0.50 μL DNA Template, 2.50 μL ddH₂O, 0.25 μL (25 pmol) forward primer, and 0.25 μL (25 pmol) reverse primer. The PCR was performed with an initial denaturation (melting double stranded DNA template into single-stranded DNA at high temperature) at 94 °C for 5 min, followed by 30 cycles of denaturing at 94 °C for 30 s, annealing at 61.8 °C for 30 s, and extension at 72 °C for 30 s. The final extension was performed at 72 °C for 10 min. The PCR product was incubated with Rsa I (TAKARA, Japan) at 37 °C overnight. According to commercial protocols, the 5.00 μL incubation system contained 1.00 μL PCR products, 4.0 U Rsa I (10 U/μL), 0.50 μL 10 × T buffer, 0.50 μL 0.1% bovine serum albumin (BSA), and 2.60 μL ddH₂O. Guided by Sambrook’s suggestion (2001), the incubated DNA fragments were separated by electrophoresis with 10% polyacrylamide gel in 200 V for 2.5 h. The gels were stained with 1.0% silver nitrate solution and developed with a solution including 2% NaOH, 0.4% Na₂CO₃, and 0.4% HCHO. Finally, the genotype bands in gels were identified by the Bio-Imaging Systems software (Bio Spectrum® 510 Imaging System, UVP, USA). In the current sample, the distribution of genotypes (AA = 193, AG = 286, GG = 115) showed no deviation from the Hardy-Weinberg Equilibrium, χ² = 0.24.
was a predictor of subjective well-being, using genotype (0 = AA, 1 = AG, 2 = GG) as the predictor and gender as a control variable, the results revealed that the G allele still significantly predicted subjective well-being on the three aspects of subjective well-being, namely SWLS, FS, and SPANE. Using genotype (0 = AA, 1 = AG, 2 = GG) as the predictor and gender as the control variable, the results revealed that the G allele still significantly predicted subjective well-being, β = 2.269, SE = 1.042, and 95% CI [0.231, 4.379].

We further conducted a 3 (Genotype: AA vs. AG vs. GG) × 2 (Gender: males vs. females) ANOVAs to investigate the impacts of CYP19A1 Val80 on the three aspects of subjective well-being, namely SWLS, FS, and SPANE. The results showed that the CYP19A1 Val80 was significantly associated with the standardized Z scores on SWLS (GG: M = 0.196, SD = 1.039; AG: M = 0.035,
SD = 0.943; AA: M = −0.168, SD = 1.036), F(2, 594) = 8.301, p < 0.001, η² = 0.027. A regression analysis with the genotypes
(0 = AA, 1 = AG, 2 = GG) as predictor revealed that the score on SWLS increased as function of number of G alleles, β = 0.131, t = 3.214, R² = 0.017, p = 0.001. The bootstrapped results (N = 500, 20,000 iterations) also showed that the G allele significantly predicted SWLS, β = 1.109, SE = 0.381, and 95% CI [0.330, 1.833]. By contrast, the genotype did not affect the standardized Z scores on FS (GG: M = 0.066, SD = 1.039; AG: M = 0.075, SD = 0.929; AA: M = −0.150, SD = 1.064), F(1, 594) = 2.589, p = 0.076, η² = 0.009, or SPANE (GG: M = 0.021, SD = 0.978; AG: M = 0.011, SD = 1.047; AA: M = −0.029, SD = 0.945), F(1, 594) = 0.717, p = 0.489, η² = 0.002. The results also indicated significant impacts of gender on the scores of FS, F(1, 594) = 8.575, p = 0.004, η² = 0.014, and SPANE, F(1, 594) = 5.943, p = 0.015, η² = 0.010, but not SWLS, F(1, 594) = 0.001, p = 0.981, η² < 0.001. Moreover, the interaction between gender and genotype on score of SWLS was significant, F(2, 594) = 4.451, p = 0.012, η² = 0.015, while the interactions on scores of FS and SPANE were absent, F(2, 594) = 0.416, p = 0.660, η² = 0.001 for FS, and F(2, 594) = 2.307, p = 0.10, η² = 0.008 for SPANE.

The correlations between subjective well-being and the environmental factors and individual characteristics are shown in Table S1 (Supplementary Materials 2). To examine whether the genetic effect on subjective well-being still existed after controlling for possible confounding variables (e.g., number of siblings, family type, caregiver type, parents’ education levels, household income, average monthly expenditures, religious beliefs, life stress, life hopes, self-efficacy, self-consistency and congruence, and mental health status), hierarchical regression analyses were performed, with the possible confounding variables and genotype as predictors and subjective well-being as the dependent variable. In Step 1, non-genetic variables were entered as predictors, and in Step 2, the genotype variable (0 = AA, 1 = AG, 2 = GG) was added as a predictor. Results showed that the contribution of CYP19A1 Val80 to subjective well-being remained significant, all ps < 0.039 (Table S2 in Supplementary Materials 2).

4.2. Mediation analysis

Our results showed that the scores on both the independent and interdependent self-construal subscales were positively correlated with subjective well-being (Table 1). As the direct effect analysis indicated a significant association between independent self-construal and CYP19A1 Val80, we examined whether the association between genotype and subjective well-being was mediated by independent self-construal. First, a regression analysis was conducted in which genotype was entered as the only predictor of subjective well-being; the results showed a significant relationship, β = 0.101, t = 2.477, R² = 0.01, p = 0.014. When both genotype and independent self-construal scores were included as predictors, the effect of genotype was no longer significant, β' = 0.069, t = 1.781, adjusted R² = 0.112, p = 0.075 (Fig. 1), of which the difference between β and β' was significant, F(1, 591) = 69.787, p < 0.001 (Neter, Wasserman, & Kutner, 1989). We bootstrapped the mediating effect 50,000 times (Preacher & Hayes, 2008) and found a significant mediating effect of independent self-construal in the relationship between CYP19A1 Val80 and subjective well-being, with mediating effect estimate = 0.0055, SE = 0.0039, 95% CI [0.0004, 0.0166]. As shown in Fig. 1, the mediating effect, which was calculated with 1-(0.069/0.101), accounted for 31.68% of the effect of CYP19A1 Val80 on subjective well-being.

5. Discussion

Testosterone and estrogen have been shown to be associated with individual differences in dominance status (Davies et al., 2016; Van Bokhoven et al., 2006), social recognition, interactional trust (Bos, Terburg, & van Honk, 2010; Ervin et al., 2015), and independent communication style (Dabbs et al., 2001). In this study, we found that the CYP19A1 Val80, a genetic polymorphism related to the conversion of testosterone into estrogen, significantly contributes to individual differences in self-construal and subjective well-being. Individuals with the GG genotype of CYP19A1 Val80, corresponding to higher testosterone levels and lower estrogen levels, described themselves as having more independent personalities and a greater sense of well-being. The link between GG genotype and independent self-construal may help explain the role of GG genotype in higher levels of self-efficacy (Dowd & Artisico, 2016), social dominance (Kupper & Zick, 2011), and aggression in human interactions (Cross & Madson, 1997). These findings provide new insights to the contributions of testosterone and estrogen to how individuals perceive, comprehend, and interpret their own behaviors; they also give a possible explanation for the psychobiological processes by which testosterone and estrogen are involved in social dominance (Sellers et al., 2007; Van Bokhoven et al., 2006), competition (van der Meij et al., 2012),

![Fig. 1. The mediation of independent self-construal in the association between CYP19A1 Val80 and subjective well-being. All estimates are standardized, with "a" indicating p < 0.05 and "b" indicating p < 0.01. Note: "a" refers to the effect of CYP19A1 Val80 on independent self-construal; "b" refers to the effect of independent self-construal on subjective well-being; "c" refers to the total effect of CYP19A1 Val80 on subjective well-being; "c'" refers to the direct effect of CYP19A1 Val80 on subjective well-being after controlling for the effect of independent self-construal.](image-url)
and aggression (Crespi, 2016) in humans.

Consistent with previous studies indicating that testosterone (Davis & Tran, 2001; Nathorst-Böös et al., 2006) and estrogen (Aziz et al., 2005; Kotz et al., 2006; Nathorst-Böös et al., 1993) replacements improve well-being in females, our study indicated that the GG genotype of CYP19A1 Val80, which is correlated with higher testosterone levels and lower estrogen levels, significantly contributes to individual differences in the extent to which participants are satisfied with their life (e.g., “In most ways my life is close to my ideal”). These findings extend our knowledge of the functions of hormones in subjective well-being. Of note, given that the heritability of subjective well-being is estimated at 38% (Stubbe, Posthuma, Boomsma, & De Geus, 2005) and the CYP19A1 Val80 only accounted for 1.0% of the variance in subjective well-being in the current study, the contribution of this polymorphism should be interpreted with caution.

In addition, the relation between genotype and well-being was mediated by independent self-construal. Similar to previous studies indicating that the evaluations of one’s life satisfaction are impacted by self-construal orientation (Duncan et al., 2013; Suh et al., 2008), we found that the association between CYP19A1 Val80 and subjective well-being is mediated by independent self-construal. The results extend our knowledge of the relationships among testosterone/estrogen levels, self-construal and subjective well-being. Although previous studies indicated that testosterone replacement improves individuals’ well-being (Davis & Tran, 2001; Nathorst-Böös et al., 2006), the underlying psychological mechanism remains unclear. The enhancements in subjective well-being may arise from contributions of testosterone to individuals’ belief in their own uniqueness and independent behavioral style in daily life.

Several limitations should be noted. Firstly, our study did not measure levels of testosterone and estrogen directly. Given the function of aromatase in converting testosterone into estrogen (Gruber et al., 2002) and given that CYP19A1 Val80 regulates aromatase, we speculate that the CYP19A1 gene influences self-construal and well-being by influencing levels of testosterone and estrogen. Further studies should directly examine the specific roles of testosterone and estrogen in these processes. Secondly, this sample was restricted to young Han Chinese individuals and whether our conclusions can be extended to other cultures and other age groups remains to be further tested. Both self-construal (Lewis, Goto, & Kong, 2008; Oyserman & Lee, 2008) and subjective well-being (Anglim, Weinberg, & Cummins, 2015; Tomas, Gutiérrez, Sancho, & Romero, 2015) show variation across cultures. Levels of testosterone/estrogen also change dramatically across age (Lamberts, van den Beld, & van der Lely, 1997; Shibayama et al., 2009). Finally, our sample size is relatively small and replication in a larger sample is needed to make definitive conclusions.

6. Conclusion

Our study delineated contributions of CYP19A1 to independent self-construal and subjective well-being. The association between the G allele of CYP19A1 Val80 and subjective well-being was mediated by a disposition toward independent self-construal. Our findings reinforce the idea that personality traits such as independent self-construal explain the link between genetic variants and subjective well-being.

Acknowledgments

We thank Shoumin Xi and Tan Zhao for their assistance with data collection.

Author Contributions

Performed the experiments: Xing Yang, Yafang Yang, Mengying Xue, Pengpeng Fang, Guomin Shen, Pingyuan Gong, Kejin Zhang, and Xiaocai Gao. Analyzed the data: Pingyuan Gong, Xing Yang, and Kejin Zhang. Wrote the paper: Pingyuan Gong, Xing Yang, and Rongjun Yu. Designed the study: Pingyuan Gong. Provided overall guidance: Pingyuan Gong.

Funding

This study was supported by grants from the Natural Science Foundation of China (31640037), Opening Foundation of Shaanxi Key Laboratory for Animal Conservation (Northwest University), and Science Research Foundation of Northwest University (338050067) to Pingyuan Gong.

Appendix A. Supplementary material

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.concog.2017.08.012.

References


