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

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

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

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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, & Gercek-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

* Corresponding author. Shaanxi Key Laboratory for Animal Conservation, Northwest University, Taibai Ave 229, Xi'an 710069, China.
E-mail addresses: gpy1026@163.com, gpy1026@nwu.edu.cn (P. Gong).

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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; McElduff & Beange, 2003; Nathorst-Böös, Flöter, Jarkander-Rolff, 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; Nathorst-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; Nathorst-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 biophysiological 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, Ornaghi, & Grazzani, 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; Somner 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; Somner 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 Somner's study showed that the GG genotype was related to lower levels of testosterone in females (Somner 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 (Somner 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 (Kashima 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.