



The relationships between androgens and novelty seeking in healthy Japanese men



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ABSTRACT

Androgens are associated with behavioral traits, such as sensation seeking, extraversion, and novelty seeking in humans and other animals. This study investigated whether the levels of total testosterone, free testosterone, and dehydroepiandrosterone sulfate (DHEA-S) in serum were associated with personality traits related to novelty seeking (NS) and its subscales in healthy Japanese male subjects ($n=178$). Novelty seeking was assessed using Cloninger's Temperament and Character Inventory (TCI). The values of the three hormones were log transformed to normalize the data and to allow the use of parametric statistics. Statistical analysis was performed using multiple stepwise regression analysis. There were no associations between the total scores of NS and total testosterone, or DHEA-S. However, free testosterone was slightly but significantly associated with extravagance (NS3), a subscale of novelty seeking. These results indicate the possibility that free testosterone has a small influence on novelty seeking in healthy Japanese male subjects, whereas total testosterone and DHEA-S have no influence. Additional TCI-based studies of the association between novelty seeking and androgens are needed to confirm our findings.

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1. Introduction

Testosterone, a male reproductive hormone produced in the testes, has been implicated in male-typical sexual behavior. Recent studies have shown that testosterone modulates the dopaminergic system and dopamine-dependent behaviors (Aubele and Kritzer, 2012; Volman et al., 2011), and some studies have reported associations between total testosterone levels and various dopamine-dependent personality dispositions. Studies of healthy subjects have reported significant associations between total testosterone and increased sensation seeking (Daitzman et al., 1978; Gerra et al., 1999; Campbell et al., 2010), extraversion (Alvergne et al., 2010), and novelty seeking (Gerra et al., 1999; Määttänen et al., 2013). Yildirim and Derksen (2012) also suggest that the association between testosterone and novelty seeking is

mediated by dopamine levels in the central nervous system. However, these results are not found in all studies (Rosenblitt et al., 2001).

Total testosterone is also reportedly associated with behaviors such as impulsivity, aggression, violence, sexual curiosity, and social disinhibition in prison inmates (Aluja and García, 2005; Giotakos et al., 2003; Dabbs et al., 1987; Studer et al., 2005). Though these findings suggest that testosterone may be associated with personality differences, most studies have only assessed total testosterone levels and have not examined the levels of bioavailable free testosterone. Several studies have reported the association of bioavailable testosterone with personality traits (Aluja and Garcia, 2005; Martin et al., 2006; Määttänen et al., 2013).

Dehydroepiandrosterone (DHEA) and its active sulfated form (DHEA-S) are precursors of testosterone that are typically secreted by the adrenal glands. DHEA exhibits a diurnal pattern (Kroboth et al., 1999), and its levels are variable because it is affected by short-term factors such as acute psychological stress (Lennartsson et al., 2012). DHEA-S has a longer half-life and lower clearance than DHEA. In addition, DHEA-S, but not DHEA, modulates *N*-methyl-*D*-aspartate (NMDA) and γ -aminobutyric acid type A (GABA_A) receptors, which may lead to the secretion of catecholamines, such as dopamine and norepinephrine, via regulation of the levels of tyrosine hydroxylase (TH) mRNA and protein (Charalampopoulos et al., 2005; Maninger et al., 2009). Therefore, it

Abbreviations: DHEA, dehydroepiandrosterone; DHEA-S, dehydroepiandrosterone sulfate; NMDA, *N*-methyl-*D*-aspartate; GABA_A, γ -aminobutyric acid type A; TH, tyrosine hydroxylase; ADHD, attention-deficit hyperactivity disorder; NS, novelty seeking; HA, harm avoidance; RD, reward dependence; P, persistence; SD, self-directedness; C, cooperativeness; ST, self-transcendence; TCI, Temperament and Character Inventory; SSS, Sensation Seeking Scale; ECLIA, electrochemiluminescence immunoassay; RIA, radioimmunoassay; PET, positron emission tomography; DRD4, dopamine receptor D4; BMI, body mass index

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is generally more clinically useful to measure DHEA-S rather than DHEA. Recent studies have reported high levels of DHEA-S in schizophrenia patients and low levels in depression patients (Heinz et al., 1999; Beyazyüz et al., 2014). Martin et al. (2006) reported that sensation seeking was correlated with DHEA-S in adolescents diagnosed with attention-deficit hyperactivity disorder (ADHD). High levels of serum DHEA-S were also found in patients with conduct disorder and aggression related to the dopaminergic system (van Goozen et al., 1998; Dmitrieva et al., 2001). Based on these studies, DHEA-S may be associated with dopamine-related personality traits. However, no studies have explored the association between DHEA-S and personality traits.

The present study aimed to examine the relationship between blood levels of total testosterone, free testosterone, DHEA-S and personality traits, with a particular emphasis on novelty seeking (NS). Personality was assessed using the Temperament and Character Inventory (TCI) (Cloninger, 1987), which is a widely used measure of personality traits. The TCI provides an assessment of personality and behavior characteristics that are affected by neurotransmitters, such as dopamine and norepinephrine; the instrument relies on a questionnaire that is based on biological theory (Cloninger, 1987). Therefore, the TCI is assumed to be a more suitable tool for examining the associations between personality traits and biological factors than other measurements, such as the Sensation Seeking Scale (SSS).

2. Subjects and methods

2.1. Participants

The participants in this study were healthy male medical students at the Hirosaki University School of Medicine. Subjects were excluded if they currently showed any neurological evidence of DSM-IV Axis I disorders. All 183 subjects were between the ages of 20 and 45. Five cases with missing data (abnormal hormone levels or incomplete data on the TCI total NS or NS subscale scores) were eliminated from the study. The analyses were therefore conducted on 178 subjects. All participants gave written informed consent. The Hirosaki University School of Medicine Ethics Committee approved this study.

2.2. Assessment of novelty seeking

Novelty seeking was measured using the Japanese version of the Temperament and Character Inventory (TCI) (Kijima et al., 1996). The TCI is a self-report questionnaire that includes 240 items. This instrument measures four dimensions of temperament, novelty seeking (NS), harm avoidance (HA), reward dependence (RD), and persistence (P) and three dimensions of character, self-directedness (SD), cooperativeness (C), and self-transcendence (ST) (Cloninger, 1987). Novelty seeking consists of four subscales, each scored separately: exploratory excitability (NS1), impulsiveness (NS2), extravagance (NS3), and disorderliness (NS4). A total score is also calculated for each dimension as the sum of the subscale scores.

2.3. Hormone measurement

A 10-mL blood sample was collected from each subject. To minimize the influence of diurnal variation, all blood samples were collected between 15:00 and 18:00. The hormone levels are most stable in the afternoon and early evening. Thus, these times are recommended for studies focusing on individual differences in the hormone levels (Gupta et al., 2000; Fukui and Yamashita, 2003; Yang et al., 2007). Serum samples were collected from

subjects and were allowed to clot for 30 min before undergoing centrifugation for 15 min at approximately 3000 rpm. The serum was stored at -80°C until it was used in the assay. The following hormones were analyzed: total testosterone (Testosterone II cobas; Roche), free testosterone (Coat-A-Count Free Testosterone; Siemens Healthcare Diagnostics), and DHEA-S (Accecc DHEA-S kit; Beckman Coulter). The respective intra-assay and inter-assay coefficients of variation (CVs) were as follows: total testosterone ($< 10\%$ and 1.2%), free testosterone ($< 15\%$ and 5.5%), and DHEAS ($< 10\%$ and 3.9%). Assay sensitivity for total testosterone, free testosterone and DHEA-S were 0.025 ng/mL , 0.15 pg/mL , $2.0\text{ }\mu\text{g/dL}$, respectively.

2.4. Statistical analysis

Because of skewed distributions, the natural logarithmic (ln) transformations were performed for the total and free testosterone and DHEA-S. Univariate analysis (Pearson's correlation) was performed to investigate the determinants of the serum total and free testosterone and DHEA-S levels. Colinearity was detected between total testosterone and free testosterone and between free testosterone and DHEA-S. Therefore, the three hormones were analyzed separately. Multiple stepwise regression analysis was performed to identify the independent determinants of the TCI scores. A value of $p < 0.05$ was considered significant. The data were analyzed using the PASW Statistics PC software for Windows, Version 18.0.0 (SPSS Inc., Chicago, IL, USA).

3. Results

Table 1 shows the descriptive values (means, standard deviations) for age, seven TCI scores, and hormone-related variables. The correlations among the hormone levels were analyzed before the correlations between the hormones and the TCI measures. There were significant correlations between total testosterone and free testosterone ($r=0.650$, $p < 0.001$) and between free testosterone and DHEA-S ($r=0.425$, $p < 0.001$), respectively. The results of the univariate analysis of the associations between the seven TCI dimensions and the levels of the three hormones are shown in Table 2. The serum total and free testosterone levels were positively correlated with NS scores ($r=0.156$, $p=0.019$, and $r=0.131$, $p=0.041$, respectively) and negatively correlated with age ($r=-0.267$ and $r=-0.256$, respectively, both $p < 0.001$). The serum DHEA-S levels were positively correlated with the ST scores ($r=0.152$, $p=0.021$) and negatively correlated with the SD scores ($r=-0.191$, $p=0.005$) and age ($r=-0.267$, $p < 0.001$). However, other than age, no significant correlation was found after the Bonferroni correction was applied (0.05/7 tests, adjusted

Table 1
Descriptive statistics of the age, seven TCI scores, and hormone levels.

Variable	Mean (Std. Dev.)
(N=178)	
Age	25.5 (3.7)
Novelty seeking	22.2 (5.7)
Harm avoidance	17.2 (6.0)
Reward dependence	14.7 (3.2)
Persistence	4.6 (1.8)
Self-directedness	29.7 (5.5)
Cooperativeness	28.9 (5.1)
Self-transcendence	8.1 (4.2)
Testosterone (ng/mL)	4.3 (1.4)
Free testosterone (pg/mL)	11.5 (4.6)
Dehydroepiandrosterone sulfate (DHEAS) ($\mu\text{g/dL}$)	394.6 (3.7)

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