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Serum Free Testosterone and Estradiol Levels in Perceptual-Verbal and Spatial Abilities; Differences in Sex and Hand Preference

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1. Introduction

Cognitive sex differences have been demonstrated in humans: men usually outperform women on spatial ability (Linn & Peterson, 1985; Gladue et al., 1990; Mann et al., 1990; Gouchie & Kimura, 1991; Gladue & Bailey, 1995; Halpern & Tan, 2001; Tan et al., 2003a, b; Herlitz & Lovén, 2009); women outperform men on verbal tasks (Hyde & Linn, 1988; Mann et al., 1990; Halpern & Tan, 2001; Tan et al., 2003a, 2003b; Herlitz & Lovén, 2009). The sex hormones were thought to be responsible for the observed sex differences in cognitive abilities, but the available scientific literature does not provide any generally acceptable conclusion on this topic. For instance, testosterone has been reported to be beneficial for visuospatial ability in men (Hier & Crowley, 1982; Gordon & Lee, 1986; Christiansen & Knusmann, 1987; Tan, 1990a, b; Tan & Akgun, 1992; Christiansen, 1993; Janowsky et al., 1994; Van Goozen et al., 1994; Van Goozen et al., 1995; Tan & Tan, 1998; Barrett-Connor et al., 1999a; Silverman et al., 1999; Aleman et al., 2001; Kutlu et al., 2001; Kenny et al., 2002; Yaffe et al., 2002; Azurmendi et al., 2005), and women (Shute et al., 1983; Resnick et al., 1986; McKeever, 1987; Gouchie & Kimura, 1991; Van Goozen et al., 1995; Moffat & Hampson, 1996; Barrett-Connor et al., 1999b; Celec et al., 2002; Ostatnikova, et al., 2002). On the other hand, testosterone has also been reported as having no benefit for spatial ability in either men or women (Shute et al., 1983; Gouchie & Kimura, 1991; Moffat & Hampson, 1996; Van Goozen et al., 1995). Contrarily, some authors did not accept any significant association between testosterone and spatial cognition (McKeever et al., 1987; Kampen & Sherwin, 1996; Herlitz & Lovén, 2009). An inverse U-shaped relation between testosterone and spatial cognition was also reported, that is, the optimal performance was found in moderately high levels of testosterone (Shute et al., 1983; Gouchie & Kimura, 1991; Moffat & Hampson, 1996; Alexander et al., 1998; Neave, et al., 1999). With regard to handedness, significant relationships have been found between testosterone and spatial ability in right-handers, but not in left-handers (Moffat & Hampson, 1996).

Verbal abilities have also been studied in relation to sex-hormone concentrations in men and women. Some authors could not demonstrate any significant association between testosterone and verbal tasks (Gordon & Lee, 1986; Gouchie & Kimura, 1991; Neave, et al., 1999; Herlitz & Lovén, 2009), but others reported beneficial effects of testosterone on verbal ability (Cherrier, 1999; Alexander et al., 1998), but detrimental influence of androgen levels

on the vocabulary ability in girls (Azurmendi et al., 2005). In female-to-male transsexuals, verbal skills have been shown to dramatically decline within three months following high doses of testosterone (Van Goozen et al., 1995). In contrast, high estrogen levels have been reported to be advantageous for verbal skills in women, and vary according to their ovarian cycle (Kimura, 1996; Halpern & Tan, 2001).

Cattell's Culture Fair Intelligence Test measuring the sex-neutral IQ (Tan et al., 1993; Tan & Tan, 1998; Halpern & Tan, 2001) shows menstrual cycle fluctuations, being lower during the pre-ovulatory and post-ovulatory phases; in fact, an inverse U-shaped relation has been found between serum estradiol concentration and Cattell IQ in women (see Halpern & Tan, 2001). Despite the sex-neutrality of this IQ test, a direct relation has been found between Cattell IQ and total serum testosterone level in left-handed men (Tan et al., 1993). An inverse U-shaped relation has also been demonstrated between the total serum testosterone level and Cattell IQ in men and women (Tan & Tan, 1998). Students successful in exams for university entrance have also been shown to have higher total testosterone than those unsuccessful in university exams (Kutlu et al., 2001). On the other hand, matrices taken from the Kaufman Brief Intelligence Test, measuring the fluid intelligence similar to the Cattell's Culture Fair Intelligence Test, showed negative correlation with serum testosterone levels in 5-year-old children (Azurmendi et al., 2005).

Tan et al. (2003a) recently reported that an observed sex difference in visuo-spatial ability was not a real sex difference but merely depended upon the body size, because with covariates of height, weight, and vital capacity, sex differences in mental rotation completely disappeared. Under a combined co-variation of height, weight, and testosterone, the sex difference in mental rotation ability reversed, women scoring better than men (Tan et al., 2003b). In perceptual-verbal ability studies (Fining As test), with covariates of estradiol and progesterone, the sex difference also disappeared, suggesting the prominent role of these sex hormones in different verbal abilities of men and women with related differences in height and weight associated with *nature vs nurture* (Tan et al., 2003b). In accord, the height and weight are correlated with brain size, which is also correlated with IQ ($r = .40$) (Rushton, 1992, 1997; Raz et al., 1993; Tan et al., 1999; McDaniel, 2005). These results suggest that the body size should also be considered as a co-variate in studies of sex-related differences in cognitive abilities.

Under light of the above mentioned controversial results about the relations of sex hormones, testosterone and estrogens, on the verbal and non-verbal, visuo-spatial abilities, the aim of the present work was to evaluate the relations of the serum free testosterone and estradiol levels to the verbal, and non-verbal, visuo-spatial ability scores in right- and left-handed men and women. Although there are numerous reports on this subject with numerous controversial results, the present work will be the first, in the scientific literature, taking only the participants within the similar range of body size in male and female young adults, following the interrelationships among the body size, intelligence, and sex hormones. Controlling the body size could help to obtain a more reliable, homogenous sample of men and women within the same age range.

2. Methods

Participants in the study were 52 male and 24 female university students. All volunteers were between 18 and 20 years old, and willing to participate in this study since they wanted to know their IQs and sex-hormone levels. They were healthy and did not exhibit neurological

signs and symptoms. Their cognitive functions were measured using three tests: "Finding As Test", "Mental Rotation Test," and "Cattell's Culture Fair Intelligence Test."

2.1 Finding As test

To measure the perceptual-verbal ability, the Finding As test from the ETS kit of Factor-Referenced Cognitive Tests (Ekstrom et al., 1976), classified as "feminine," was administered to the subjects. The test-retest correlation has been reported to be $r = .87$ for this test (Ekstrom et al., 1976). This test is usually used to assess the perceptual speed, and favors women, with very large effect size (Jensen, 1998 and e.g., Kimura & Hampson, 1994; Halpern & Tan, 2001; Tan et al., 2003b).

In each column of 40 words, the respondents were required to identify the five words containing the letter "a." In the Turkish version of this test (see Halpern & Tan, 2001), the subjects were asked to read the words in several columns as fast as possible, and cross out the letter "a" whenever it appears in the word list. This is a timed test of two minutes was allowed to read one page out of three pages, which the subjects should examine consequently. After completing the test, the number of the correctly chosen words was determined for each subject.

2.2 Mental Rotation Test (MRT)

To study mental rotation functions and the ability to solve spatial problems, the "Mental Rotation Test" (MRT) was used. This test was originally developed by Vandenberg and Kuse (1978), based on a design by Shepard and Metzler (1971). This test is a timed, group-administered paper-and-pencil test comprising problems in which participants are required to say whether pairs of two- or three-dimensional drawings of cubes from different angles and perspectives were the same or mirror images of each other. There were 25 problems, giving a maximum possible score of 25.

2.3 Cattell nonverbal intelligence test (Test of "g": Culture Fair)

The Cattell's Culture Fair Intelligence Test was originally designed to be a general measure of inborn intelligence without utilizing verbal material (Cattell, 1973, 1987). We applied the Institute for Personality and Ability (IPAT) Culture Fair Intelligence Test, Scale 3A, Form A to university students. The test primarily measures fluid intelligence, with part-whole relations, similarities, causal and spatial relations, inductive reasoning, inferential relations, including series, classification, matrices, and topology. There were 13 items on Subset 1 (3 min), 14 items in Subset 2 (4 min), 13 items in Subset 3 (3 min), and 10 items in Subset 4 (4 min). Raw scores were converted to normalized scores expressed by age group, and scoring was performed by using score key overlays with the response forms. Factor analysis showed validity in the 1970s and 1980s when the general ability factor was correlated with the concepts featured in the subtests (see Cattell, 1987). The spatial ability seems to be the most important factor with some loading on verbal and numerical abilities.

2.4 Hormone tests

Following the tests for cognitive abilities, blood was taken from the cubital vein the same day, and stored in the deep freeze for later analysis of hormone concentrations. The serum free testosterone and estradiol concentrations were measured using a radioimmunoassay technique (Diagnostic Product Corporation, USA), which is commercially available. Because

testosterone shows diurnal and circadian variations (Kimura & Hampson, 1994; Moffat & Hampson, 1996), all the tests were completed and blood samples were taken before noon in the spring semester (May).

3. Results

3.1 Sex hormone levels

The mean testosterone levels were found to be 7.56 ± 2.7 ng/dL and 5.2 ± 3.7 ng/dL for the right-handed men (N = 33) and left-handed men (N = 19), respectively. The difference between these means was statistically significant: $t = 2.67$, $df = 50$, $p = .01$. There was no significant difference between the mean estradiol levels of the right-handed (28.26 ± 15.04 pg/mL) and left-handed (29.16 ± 14.93 pg/mL) male subjects, $t = 0.21$, $df = 50$, $P > .80$. The number of the left-handed females was not statistically suitable to make any comparison with right-handed women.

3.2 Mental rotation ability

Test	N	Mean	Minimum	Maximum	25%-75%
Mental rotation					
RH males	29	10.55 ± 3.40	5.00	20.00	8.00-13.25
RH females	24	8.17 ± 3.12	3.00	16.00	5.50-10.00
LH males	19	8.16 ± 3.18	2.00	8.00	6.00-10.75
Cattell					
RH men	25	115.8 ± 6.6	104	128	108-120
RH women	18	117.9 ± 8.3	106	133	114-124
As					
RH men	25	37.9 ± 5.4	27	47	33-42
RH women	20	$40.7 \pm .9$	23	59	35-46

Table 1. Mental rotation, Cattell IQ and Finding As Test results

3.3 Sex hormones

3.3.1 Right-handers

Figure 1 illustrates the relation between serum testosterone and estradiol levels (abscissa) and mental rotation ability (ordinate) in the right-handed men (A, B) and women (C, D). In right-handed men, the relation between serum testosterone level and the number of correct answers on the mental rotation test could be best described by a quadratic equation (Figure 1A), i.e., the lowest mental rotation scores were at both ends of the inverted U-shaped curve. This quadratic relation was statistically significant: $r = .61$, $F(1, 24) = 7.7$, $p < .001$. In right-handed women, there was a direct relation between serum testosterone level and mental rotation scores, $r = .61$, $F(1, 22) = 13.2$, $p < .001$ (Figure 1C). The serum estradiol level directly correlated with mental rotation test scores in the right-handed men (Figure 1B); the relation was statistically significant, $r = .61$, $F(1, 24) = 13.9$, $p < .001$. Similar to testosterone versus mental rotation in right-handed men, there was a quadratic relation (inverse U) between serum estradiol level and mental rotation ability in right-handed women, $r = .57$, $F(1, 22) = 5.3$, $p < .05$ (Figure 1D).

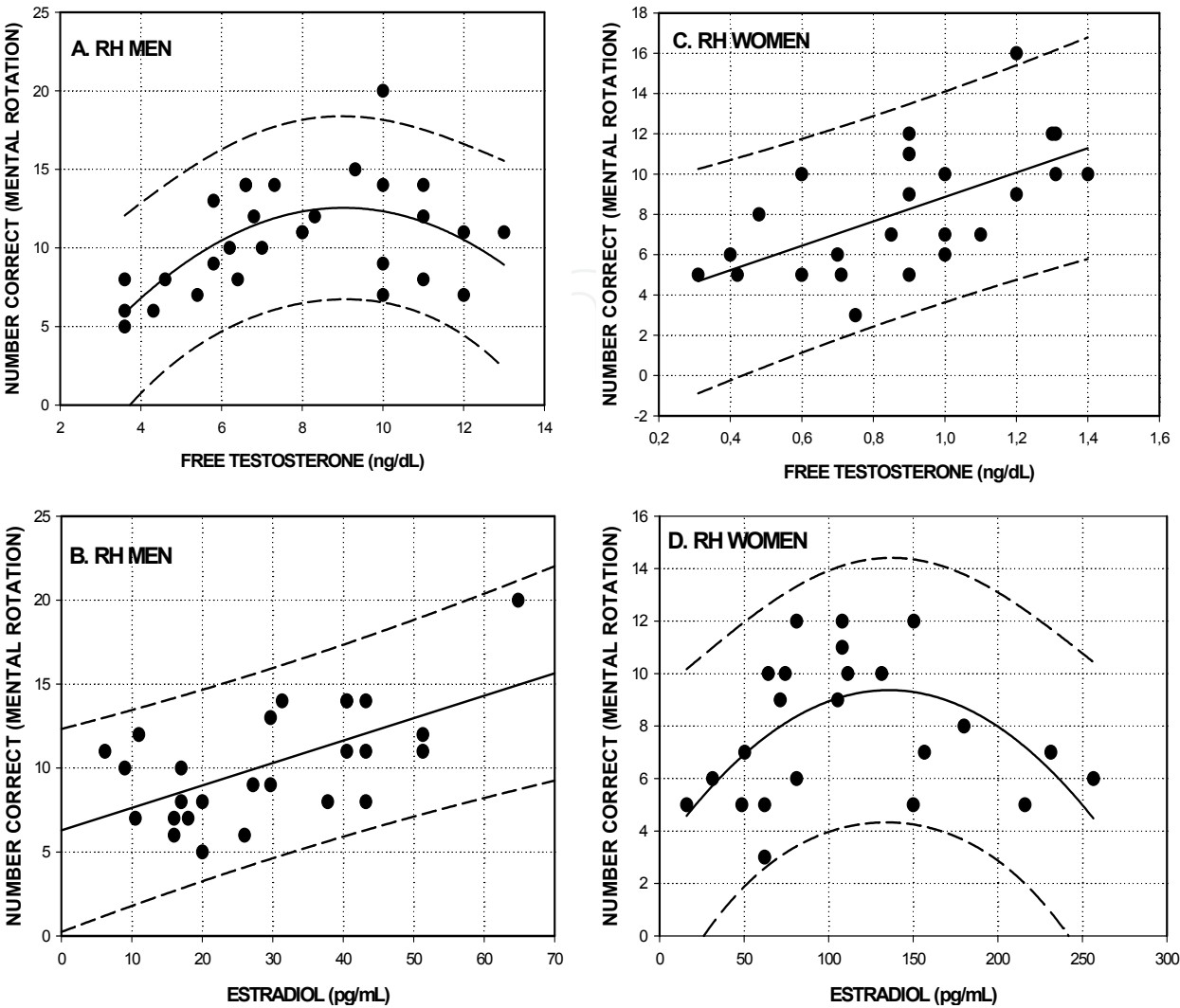


Fig. 1. Relations of serum testosterone and estradiol concentrations (abscissa) to mental rotation test scores (ordinate) in right-handed men (A, B) and women (C, D).

3.3.2 Left-handers

The scattergrams in Figure 2 illustrate the variations in mental rotation scores (ordinate) with various serum testosterone (left) and estradiol (right) levels in left-handed subjects. Since there were only a few left-handed females ($N = 6$), all left-handers were analyzed together (Figure 2), and the results were essentially similar to the right-handed male subjects. The relation of mental rotation ability versus testosterone could best be described by a quadratic equation, $r = .49$, $F(1, 17) = 5.5$, $P < .05$, with a slight decrease in mental rotation ability towards the higher testosterone levels. The relation of mental rotation to estradiol was best described by a direct correlation, $r = .68$, $F(1, 17) = 14.3$, $p < .001$.

3.4 Cattell's culture fair intelligence test

There was no significant sex difference in Cattell IQ, $F(1, 161) = 0.31$, $p > .55$. Since there were only a few left-handed subjects who took the Cattell IQ test, only the right-handers will be analyzed in this section. Figure 3 illustrates the relation between the serum testosterone and estradiol levels (abscissa) to Cattell IQ (ordinate) in the right-handed male

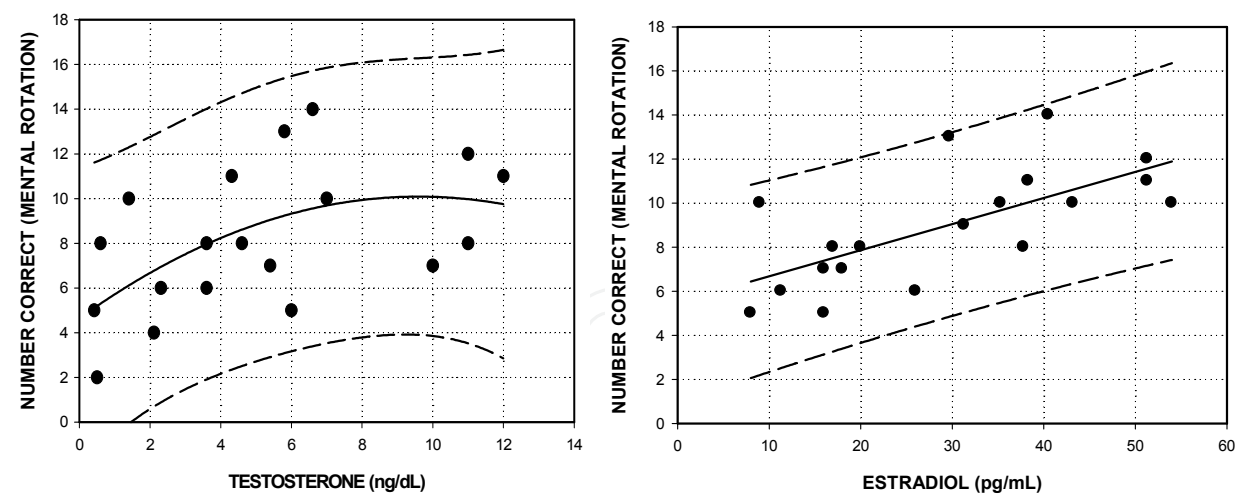


Fig. 2. Relations of mental rotation test scores (ordinate) to serum testosterone (left) and estradiol (right) levels in left-handed subjects.

(A, B) and female (C, D) subjects. In males, there was no significant correlation between testosterone and IQ (Figure 3A; $r = .00$; $N = 25$). The relation between estradiol and IQ could best be described by a quadratic (inverse U shaped) function (Figure 3B). This relation was found to be statistically significant ($r = .47$, $F = 7.2$, $p < .05$).

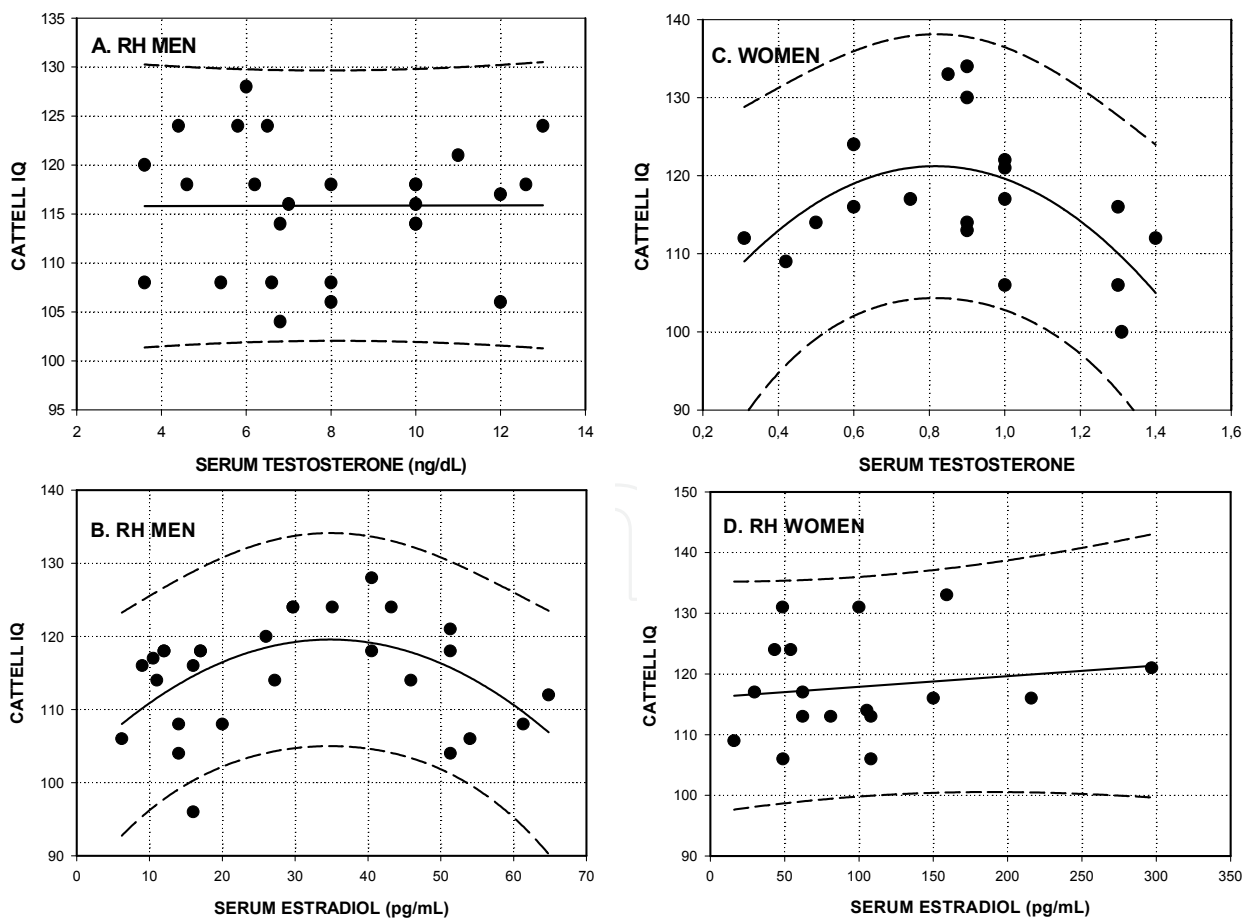


Fig. 3. Relations of serum testosterone and estradiol levels (abscissa) to Cattell IQ (ordinate) in male (left) and female (right) right-handed subjects.

An opposite picture was found for the female subjects. Namely, there was a quadratic, inverse U-shaped relation between testosterone and IQ (Figure 3C; $N = 16$, $r = .55$, $F = 7.3$, $p < .05$), and there was no significant correlation between estradiol and Cattell IQ (Figure 3D; $N = 16$, $r = .15$, $F = 0.4$, $p > .55$).

3.5 Perceptual-verbal ability (“Finding As Test”)

3.5.1 Right-handers

Figure 4 illustrates the relation between the number of correct answers on the “Finding As Test” (ordinate) to the serum testosterone and estradiol levels (abscissa) in right-handed male (A, B) and female (C, D) subjects.

There was an inverse relation between the serum free testosterone levels and the number of correct answers, and this was best described by a quadratic relation, $r = .73$, $F = 12.9$, $p < .001$ (see Figure 4A). The serum estradiol level exhibited an inverse U-shaped (quadratic) relation to the perceptual-verbal ability ($N = 25$, $F = 19.3$, $p < .001$). In right-handed female subjects, the serum testosterone level significantly correlated with the numbers of correct answers on the test (see Figure 4C; $r = .53$, $F = 7.1$, $p < .05$). The relation between serum estradiol level and the number of correct answers was inverse U-shaped (Figure 4D; $r = .57$, $F = 9.0$, $p < .01$).

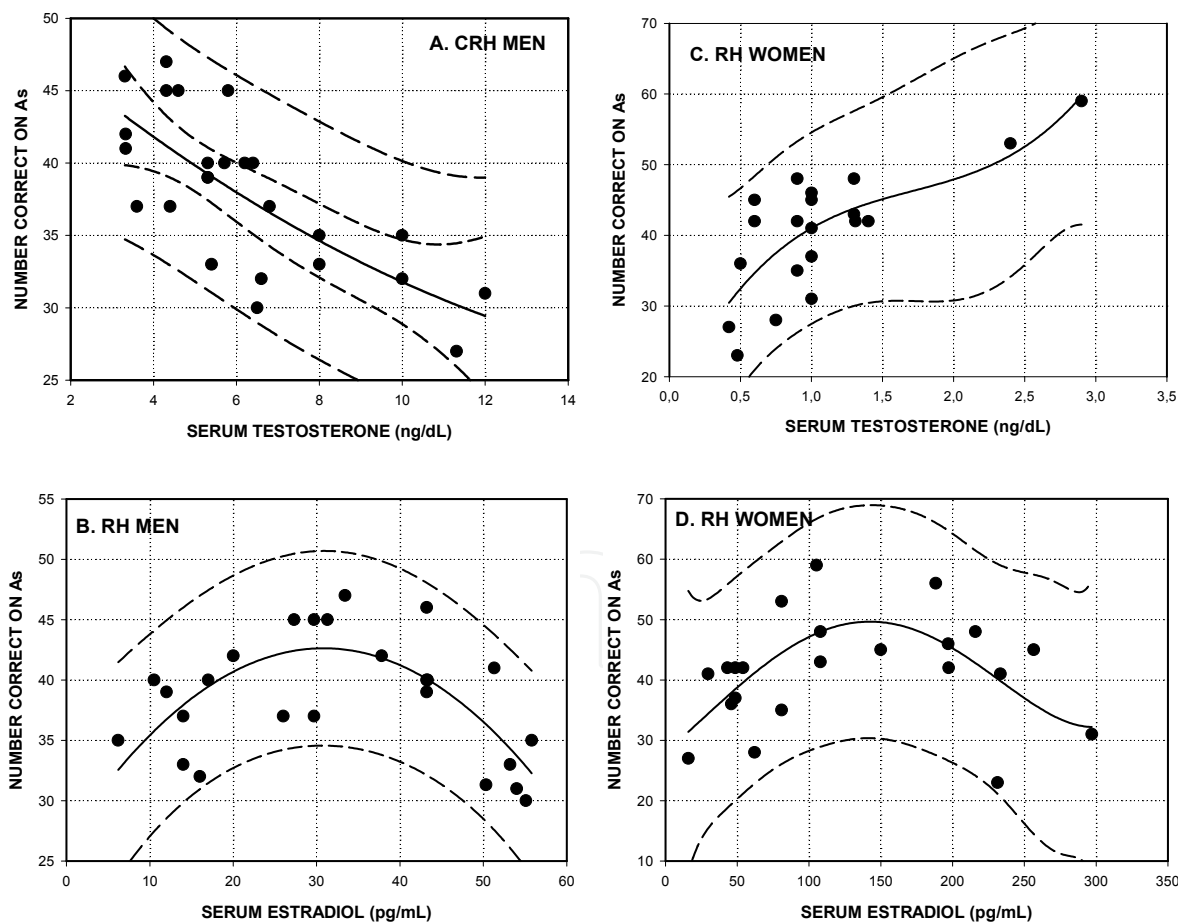


Fig. 4. Relations of number correct on As (ordinate, perceptual-verbal ability) to serum testosterone and estradiol levels (abscissa) in right-handed male (left) and female (right) subjects.

3.5.2 Left-handers

Since there were so few left-handed females, only the male left-handers were analyzed. Figure 5 illustrates the relation between the serum free testosterone and estradiol levels and the number of correct answers on the “Finding As Test”. There were positive correlations between the number of correct answers and the serum testosterone and estradiol levels in these subjects. The correlation between the number of correct answers and serum free testosterone level was best described by a quadratic equation: $r = .62$, $F(2, 15) = 12.1$, $p = .001$; the serum estradiol level was positively linearly correlated by the equation: $r = .88$, $F(1, 12) = 20.0$, $p < .001$.

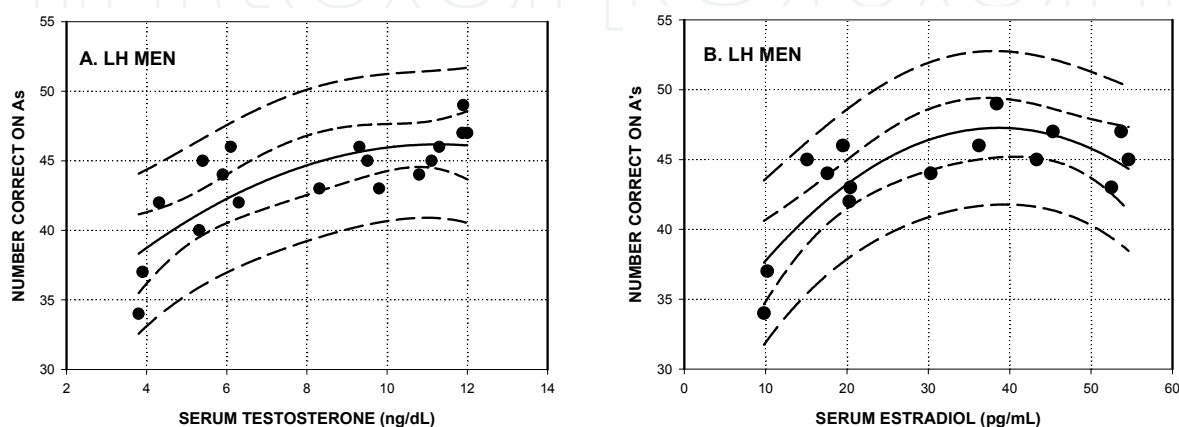


Fig. 5. Relations between perceptual-verbal ability (ordinate: number correct on A's test) and serum free testosterone (A) and estradiol (B) levels in left-handed male subjects.

4. Discussion

4.1 Mental rotation ability

The results suggest that testosterone may be beneficial for mental rotation ability in women (see Figure 1C). Moffat and Hampson (1996) also found a positive correlation between visuospatial performance and salivary testosterone level in right-handed females, but there was no significant correlation in left-handed females. The sample size for the left-handed women was not large enough in the present work to make any statistical inferences.

The beneficial effects of testosterone on spatial ability has also been experimentally verified in humans and animals. Aleman et al (2004) found that a single testosterone administration improved mental rotation ability in young women; Roof and Havens (1992) found in rats that males outperformed females in the Morris water maze (spatial ability), and females given testosterone performed better than females without testosterone.

In right- and left-handed men, the mental rotation ability increased with testosterone for a large testosterone spectrum, but tended to decrease with very high testosterone levels, which was especially visible in right-handers (see Figures 1A and 2). In contrast to women, there are inconsistencies in the scientific literature with regard to testosterone effects on spatial ability in men. Some authors found a direct correlation, while others found an inverse relation, or an inverse U-shaped relation. The present work suggests relatively high testosterone levels would be advantageous, but very low and very high testosterone levels would be disadvantageous for the mental rotation ability in right- and left-handed men.

The present results favor the hypothesis that serum free testosterone is beneficial for visuospatial ability for a large part of the testosterone spectrum regardless of hand

preference. Consistent with a curvilinear relation, Beech (2001) found that moderate baldness reflecting high levels of blood dihydrotestosterone is related to better performance in the mental rotation test in males. Supporting the dominant beneficial effect of testosterone on spatial ability in men, Christiansen and Knussman (1987) found a positive linear correlation between testosterone (salivary and serum) and spatial performance. There are many other examples supporting beneficial testosterone effects on spatial ability, such as in female-male transsexuals (Van Goozen et al., 1994), older men (Janowsky et al., 1994, 2000), and hypogonadal men (Alexander et al., 1998). According to Silverman et al. (1999), mental rotation scores are positively correlated with mean testosterone levels, but not with changes in testosterone. Gonadectomized male rodents have been shown to exhibit reduced cognitive performance (object recognition, radial arm maze, testosterone-maze, inhibitory avoidance), which could be reversed by testosterone-replacement (Frye et al., 2003). There are also inconsistent reports of low salivary testosterone levels being advantageous and high salivary testosterone levels being disadvantageous for visuospatial ability (Gouchie & Kimura, 1991; Moffat & Hampson, 1996). There are also studies showing null relations (e.g., McKeever et al., 1987; McKeever & Deyo, 1990).

The possible reasons for these inconsistencies may be diverse sample characteristics such as differences in educational levels (see Kutlu et al., 2001), hand preferences, and different measurement techniques (e.g., salivary versus serum testosterone levels), which, however, may not be related to inconsistent results, according to Silverman et al. (1999). On the other hand, differences in body size may also play a role in inconsistent results (Tan et al., 2003a, 2003b). The results of the present work suggest that serum free testosterone may be beneficial for the mental rotation ability in men and women, except that when levels of testosterone are too high in men there is a detrimental effect on mental rotation ability.

The relation of estradiol to mental rotation ability exhibited an inverse U-shaped relation to serum estradiol levels in right-handed women (Figure 1D), similar to that found in right-handed men as shown in Figure 1A. On the other hand, estradiol positively linearly correlated with mental rotation in right- and left-handed men (see Figures 1B and 2), like testosterone in right-handed women (Figure 1C). Inconsistent with these results, Wolf and Kirschbaum (2002) could not find a significant relation between endogenous estradiol levels and mental rotation in older men and women, suggesting no beneficial effects of estradiol in older people. There are, however, studies suggesting that high estradiol levels may be disadvantageous for spatial ability, consistent with the present results. For instance, in elderly women high estrogen levels showed negative relations to visuospatial functions (Drake et al., 2000; Barrett-Connor & Goodman-Gruen, 1999); performances on spatial tasks are hindered in the midluteal phase of the menstrual cycle as well as during pregnancy (Hampson, 1990; Hampson & Kimura, 1988; Maki et al., 2002; Silverman & Phillips, 1993). The inverse U-shaped variation of mental rotation ability is best seen during the menstrual cycle, parallel with the endogenous estradiol concentrations (see Figure 6 in Halpern & Tan, 2001). The above mentioned studies suggesting disadvantageous effects of high estradiol (E2) levels on spatial cognition in women support the present results. There are, however, advantageous effects of estradiol in relatively moderate concentrations; very low E concentrations were associated with low mental rotation scores (see Figure 1D). Beneficial effects of estrogen replacement therapy have frequently been reported, especially in post-menopausal women and in women with Alzheimer's disease (see Yaffe, Lui et al., 2000), so an optimal estradiol level would be most beneficial, but too much estradiol would be harmful for the spatial ability in women. The same was true for men in relation to serum testosterone levels, as seen Figure 1A.

These two relations partly support Nyborg's (1983) optimal gonadal hormone theory, which argues that there is an inverted U-shaped relationship between brain estrogen and spatial ability, with males tending more than females to occupy the peak of the curve. Nyborg assumed, however, that testosterone does not affect the brain directly, but exerts its effects by aromatization to estrogen in the brain.

There was a positive correlation between serum estradiol level and mental rotation ability in the right-handed male subjects (see Figure 1B) and this suggests that estradiol is beneficial for the mental rotation ability in men. The free testosterone level was also found to be beneficial for this ability for a large spectrum of testosterone levels. Consequently, the positive relation of serum estradiol level to mental rotation ability is to be expected, since testosterone is a circulating pro-hormone, which, through aromatization, is converted to E2, the principal ligand for estrogen receptors (see Simpson, et al., 2002). The male estradiol should be very important, since men maintain a high circulating level of the active precursor testosterone, which is available for conversion to estradiol (estradiol, or active estrogen) throughout life in extragonadal sites.

The activating effects of testosterone and estradiol on the mental rotation ability was also observed in left-handed male subjects (see Figure 2), in contrast to the results of Moffat and Hampson (1996), who could not find any relation of testosterone to spatial ability either in left-handed males or in left-handed females.

Jordan et al. (2002) have reported that women and men exhibited activations in different cortical areas during mental rotation even when performances were similar. This suggests the sex-related differences in the relations between sex hormones and mental rotation ability may be accounted for by different cerebral origins of the visuospatial abilities.

4.2 Cattell's culture fair intelligence test

There is no significant sex difference in Cattell IQ (see also Tan et al., 2003 a, b). Despite that, there were some significant relations between sex hormones and IQs. The results did not support the notion that there is no relation between testosterone and performance on some cognitive abilities at which men are not usually better (Gouchie & Kimura, 1991). The fluid intelligence, as measured by Cattell's Culture Fair Intelligence Test, has frequently been reported to be related to serum total testosterone levels in men and women (Tan, 1990 a, b; Tan & Akgun, 1992; Tan et al., 1993).

Although Cattell's Culture Fair Intelligence Test also measures the visuospatial ability, which is similar to mental rotation ability, the relations between testosterone and estradiol to Cattell IQs were quite different from those for the mental rotation test (see Figure 3). So, different visuospatial tests may produce different results. Here again, the correlations exhibited sex-dependent results: there was no significant relation between testosterone and IQ in males, and no significant relation between estradiol and IQ in females. testosterone in women and estradiol in men exhibited curvilinear correlations with Cattell IQ. These results suggest the possible effects of testosterone and estradiol on Cattell IQ may reflect the independent, direct effects of these sex hormones on nonverbal intelligence. The differential sex-related correlations may be due to the sex-related cortical activation patterns as for the mental rotation task (see Jordan et al., 2002).

The results are good examples for the optimal hormone levels for the highest cognitive abilities. Halpern and Tan (2001) showed fluctuations in Cattell IQ with menstrual cycle, and found an inverse U-shaped relation between serum estradiol level and Cattell IQ using a larger sample size. Using the total serum testosterone level, Tan and Tan (1998) reported there were

curvilinear correlations (close to inverse U) between testosterone and Cattell IQ, especially in young women. The present results showed the relations of serum free testosterone vs Cattell IQ in men, and serum estradiol vs Cattell IQ in women were insignificant, but the relations of testosterone to Cattell IQ in women, and estradiol to Cattell IQ in men showed inverse-U shaped relations (see Figure 3). So, only optimal estradiol concentrations in men and optimal testosterone concentrations in women are beneficial for this visuospatial ability.

4.3 Perceptual-verbal ability ("Finding As Test")

The finding As test is a perceptual-verbal test, usually yielding higher scores for females than males (e.g., Kimura & Hampson, 1994; Halpern & Tan, 2001). In the current study this test also exhibited sex-related differential correlations with testosterone and estradiol (see Figure 4). In left-handed male subjects, testosterone and estradiol levels showed positive correlations with the score on the test, but the relations were different in right-handers. The results were inconsistent with Gouchie and Kimura (1991) who reported that sex hormones may not influence mental ability tests that favor women or do not typically show a sex difference. Interestingly, Tan et al. (2003a) have reported the sex difference on the Finding As Test increased using testosterone as covariate; but disappeared with covariates of estradiol and progesterone, suggesting the remarkable dependence of this test on hormonal milieu.

Serum free testosterone level was inversely related to perceptual-verbal ability in right-handed men: increasing testosterone levels seemed to be detrimental (Figure 4A). Van Goozen et al. (1994) have also found that verbal fluency deteriorated after testosterone levels were increased into the physiological range for men. Alexander et al. (1998) could not find any significant association between testosterone and perceptual speed in this test in eugonadal and hypogonadal men.

In women, there was a positive relation between testosterone and perceptual-verbal ability: the score on the test increased with serum free testosterone levels (Figure 4C). In support, Drake et al. (2000) reported that higher testosterone levels were associated with superior verbal fluency in older women. A positive correlation was also found between testosterone and verbal memory in healthy elderly women (Wolf & Kirschbaum, 2002). It was argued that high levels of male sex steroids may impair performance on tests in which women outperform men (see Almeida, 1999; Wolf et al., 2000). In the present work, women outperformed men in the Finding As Test, but, despite that, testosterone was not detrimental; rather it seemed to be beneficial for this ability.

Interestingly, there was an inverse U-shaped relation between estradiol and the Finding As Test score in right-handed males and females. This means there is an optimum estradiol level for this perceptual-verbal ability, as also shown for the pre-ovulatory phase of the menstrual cycle, where serum estradiol level first increases and then decreases towards the ovulation (see Figure 5 in Halpern & Tan, 2001). So, advantageous and disadvantageous effects of estradiol are both recorded in the scientific literature.

The serum testosterone and estradiol levels were found to be positively correlated with the perceptual-verbal ability in the left-handed male subjects (Figure 5). There is no report from the current literature to compare the present results on this topic. The results suggest opposite relations of serum testosterone and estradiol levels to the perceptual-verbal ability in right- and left-handers, accentuating the importance of cerebral laterality in sex-hormone relations to cognitive abilities.

The scientific literature abounds with examples of hormonal effects on various abilities. For example, estrogen was found to have a possible positive effects on oral reading in post-menopausal women (Shaywitz et al., 2003), but an association between estrogen level and

verbal memory has not been generally supported (see Green et al., 2000). Wolf & Kirschbaum, (2002) have indeed shown that in older women higher estradiol levels were associated with better verbal memory (paired associates). Anti-androgen therapy in combination with estrogen treatment was shown to have no enhancing effect on verbal fluency in adult men (Slabbekoorn et al., 1999). Women were shown to have enhanced verbal articulation during the pre-ovulatory phase of the menstrual cycle when only estrogen levels were high (Hampson, 1990). Manipulations of sex hormone levels appeared to be unrelated to verbal skills and perceptual speed in transsexuals (Slabbekoorn et al., 1999), while in menopausal women estrogen replacement therapy have been shown to improve cognition, especially verbal memory (Wolf, 2003). Serum free and bioavailable estradiol may have beneficial effects for cognitive decline in older women (Yaffe, Haan et al., 2000), but this benefit may be obtained with a low dose of estrogen (Tierney, 2000).

5. Conclusions and perspectives

Since the most prominent sex difference in mental rotation ability – being better in men than women – reversed under covariation of bodily measures such as height and weight, to be better in women than men, and similar changes were observed in other cognitive tests, the sex differences in perceptual-verbal and spatial abilities were re-studied in the present work, which recruited men and women with similar height and weight and with known right- or left-hand preference.

The mental rotation ability predominantly increased with serum free-testosterone levels in right- and left-handed men and women, but there were detrimental effects of very large testosterone concentrations in the same individuals. The serum estradiol concentrations showed a direct relationship to mental rotation test scores in right- and left-handed men, but an inverse U-shaped relation in right-handed women. The relation of perceptual-verbal ability *vs* testosterone exhibited a different pattern: in right-handers the correlation was negative, while in left-handers it was positive. This suggests an optimum estradiol level could be beneficial for this ability in men and women.

The sex-neutral Cattell IQ did not show any significant relationship either to the serum testosterone level in right-handed men or to the estradiol level in right-handed women. Optimal testosterone and estradiol levels (not too high and not too low) were needed for the highest Cattell IQs in right-handed men and women, but if levels of these hormones were too high or too low this was detrimental for the sex-neutral fluid intelligence.

The results of the present work suggest that the sex-related differences in cognitive abilities may depend upon the hand preference and the cognitive tests used to measure the cognitive abilities. Sex-hormones may exert beneficial or detrimental effects on the cognitive abilities, depending upon their serum concentrations and cerebral laterality differences. The results also suggest that bodily measures, hand preference, and sex as basic variables should be considered in basic research and clinical evaluations, as well as in future treatment for cognitive impairments and related cognitive disorders such as dementia in men and women. The results may also be enlightening for future research on the physiological mechanisms of cognitive abilities.

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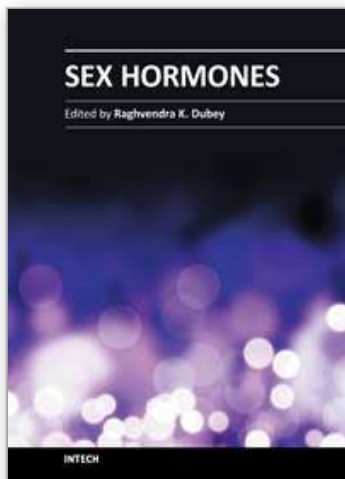
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Sex Hormones not only regulate reproductive function, but they also play a prominent role in the biology and physiology of several organs/tissues and in the pathophysiology of several diseases. During the last two decades, the information on the mechanisms of action of sex hormones, such as estrogens and androgens, has rapidly evolved from the conventional nuclear receptor dependent mechanisms to include additional non-nuclear, non-genomic and receptor-independent mechanisms. This highlights the need to update the current knowledge on sex hormones and their mode of action. Increasing evidence that exogenous/epigenetic factors can influence sex hormone production and action highlights the need to update our knowledge on the mechanisms involved. This book provides a systematic and updated overview of the male/female sex-hormones and their impact in the biology and physiology of various organs. Additionally, the book discusses their positive and negative association with the pathophysiology of various diseases (e.g. osteoporosis, cardiovascular-disease, hypogonadism, reproduction, cancer) and their therapeutic potential.

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