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Research paper

Sex steroids and personality traits in the middle luteal phase of healthy normally menstruating young professional women

Pavlina D. Avgoustinaki[1], Effrosyni Mitsopoulou[2], Gregorios Chlouverakis[1], Theoni Triantafillou[3], Maria Venihaki[1], Sofia Koukouli[4], Andrew N. Margioris[1]

[1]Departments of Clinical Chemistry and Biostatistics, School of Medicine, University of Crete, Greece, [2]Department of Psychology, University of Amsterdam, The Netherlands, [3]Psychiatric Clinic, 414 Military Hospital, Athens, [4]Department of Social Work, School of Health and Social Welfare, Technological Educational Institute of Crete, Greece

ABSTRACT

OBJECTIVE: Sex steroids affect human behavior. The aim of the present study was to determine the associations, if any, between the circulating levels of gonadal and adrenal sex steroids in the mid luteal phase (21st day of a normal menstrual cycle, MC) of young professional women and psychometric parameters as assessed by the Minnesota Multiphasic Personality Inventory (MMPI). RESULTS: Our results are as follows: (a) The metabolic product of activated adrenal and gonadal androgens, 3alpha-diolG, was modestly but significantly associated with the social introversion scale (10-SI) ($r=0.36$, $p<0.05$), independently accounting for 13% of its variation across participants ($R^2=0.13$, $F(1,45)=6.58$, $p=0.014$). (b) Total testosterone was significantly associated with the paranoia scale (6-Pa) ($r=0.27$, $p<0.05$). Multiple regression analyses indicated that 10% of the variability in paranoia scores could be independently explained by total testosterone levels ($R^2=0.10$, $F(1,57)=6.23$, $p=0.016$). We were unable to find any association between the circulating androgens and scores on the masculinity-femininity scale (Mf). We were also unable to document any association between the weak adrenal androgens DHEA and DHEA-S and depression in contrast to several published reports. (c) Our data suggest a marginally significant association between progesterone and scores on the 7-Pt (obsessive/compulsive/psychasthenia) scale ($r=0.27$, $p<0.05$). However, only 7% of the 7-Pt variance was explained by progesterone ($R^2=0.071$, $F(1,50)=3.81$, $p=0.057$). CONCLUSIONS: We have found that total testosterone was associated with the paranoia score, the metabolic product of activated androgens, 3alpha-diolG, to social introversion and, finally, progesterone to obsessive-compulsive behavior.

Key words: 3alpha-androstendiol-G (3alpha-diolG), Menstrual cycle, Minnesota Multiphasic Personality Inventory (MMPI), Obsessive-compulsive behavior, Progesterone, Social introversion, Testosterone

Address for correspondence:
Pavlina D. Avgoustinaki, Department of Clinical Chemistry - Biochemistry, School of Medicine, University of Crete, Heraklion GR-710 03, Crete, Greece, Tel.: 30-2810-394588, Fax: 30-2810-394581, E-mail: andym@med.uoc.gr

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INTRODUCTION

In pre-menopausal women, the levels of circulating sex steroids (gonadal and adrenal) have been linked to several psychological parameters. For example, the circulating levels of progesterone, a major gonadal sex steroid peaking in the luteal phase of normal menstrual cycles, are associated with increased frequency of an unusual type of compulsive cleaning behavior and other obsessive manifestations as well as with a well-documented preference for "feminine" behavioral patterns and strong commitment to established relationships.[1-5] In addition, self-reported negative mood or bona fide depression has been shown to peak during the luteal phase of the menstrual cycle (MC).[6] Furthermore, the sudden decline of serum progesterone following delivery has been repeatedly implicated in the etiology of postpartum blues.[7] It is of note that some of the behavioral effects of progesterone have been attributed to progesterone-mediated changes of inter-hemispheric communication. It has indeed been proposed that the high levels of progesterone during the luteal phase of the MC lead to a transient functional decoupling of the cerebral hemispheres.[8] However, in naturally cycling women, the levels of salivary progesterone do not appear to correlate with currently available indices of inter-hemispheric communication.[9]

As with progesterone, the levels of circulating adrenal and gonadal androgens in women have been linked to several aspects of sexual behavior, cognition, sense of well-being, depression, assertiveness, aggression and manual dexterity.[10] More specifically, testosterone levels correlate with depressive symptoms in a wide range of ages, from young healthy pubertal girls to post-menopausal women.[11-15] Likewise, high testosterone levels in young women are associated with self-directed, action-oriented, aggressive personality traits.[16,17] Conversely, lower testosterone levels are associated with non-aggressive and more traditional feminine personality traits.[18,19] High testosterone levels in young women appear, furthermore, to be associated with better spatial and mathematical abilities[20] but with lower scores on maternal and reproductive ambition.[21] Similarly, the weak adrenal androgens dehydroepiandrosterone (DHEA) and its sulfate derivative DHEA-S have been associated with an expansive and egocentric personality, as assessed by the MMPI-1 questionnaire.[22] Testosterone and DHEA-S are also associated with depression, at least in post-menopausal women.[23,24] It should be mentioned, however, that several older studies were unable to document any correlation between androgen levels and distinct personality characteristics. For example, in a study of German women no correlation was found between serum testosterone or its metabolic product in urine, the 17-ketosteroids and personality traits.[25] Similarly, no correlation was evident between serum androgens and clinical measures of psychopathology in hirsute Italian women.[26] It should nevertheless be pointed out that these early biochemical parameters of the female endocrine milieu display low sensitivity and specificity.

The aim of the present study was to examine whether the circulating gonadal and adrenal sex steroids during the 21st day (luteal phase) of normal ovulatory MCs in young, healthy women (with no clinical or laboratory evidence of hyper-androgenism or hirsutism and not using oral contraceptives) reveal any association with psychological traits as evaluated by the MMPI-1.

SUBJECTS AND METHODOLOGY

Participants, Setting and Procedures

Fifty-nine health professionals working at the University of Crete Medical School and adjoining Hospital, aged 17 to 34 years (M = 23.86 years, SD = 3.45), participated in the study. Care was taken to ensure a homogeneous sample in terms of social, professional and educational characteristics. Indeed, the participants were working either as Registered Nurses (RN), medical students or post-graduate MDs in specialty training. All participants fulfilled the following criteria: they did not use oral contraceptives or any other medication; they did not have MC irregularities, hirsutism, polycystic ovaries, unovulatory cycles (screened using progesterone levels) or history of other medical problems. Blood drawing, questionnaire completion and clinical examination were performed on the same day for each participant (i.e. the 21st day of the MC). In our population of young, healthy, professional, normally menstruating women, the length of the menstrual period, i.e. from first day of bleeding to the first day of the next men-

strual bleeding, was 28-29 days. Day 21 was selected for our measurements since it is in the middle of the luteal phase of the cycle characterized by the highest concentration of serum progesterone, an established indicator of ovulation. In normally ovulating women, seven to eight days post ovulation serum progesterone is usually more than 10 ng/mL.[27-29]

The following gonadal and adrenal sex steroids were measured: serum total testosterone, serum free testosterone, the metabolic product of activated androgens 3alpha-androstanediol glucuronide (3alpha diolG), Delta 4-Adrostendione, the weak adrenal androgens DHEA and DHEA-S in serum, 17 hydroxy-progesterone (17OHP to exclude any steroidogenetic enzyme abnormalities), progesterone and estradiol. Finally, the gonadotropins LH and FSH and prolactin were also measured. The clinical evaluation for possible hyper-androgenism or hirsutism included scores on the semi-quantitative Ferriman-Galway scale. Participation in the study was voluntary and participants were informed that all results were confidential.

Personality assessment

The Minnesota Multiphasic Personality Inventory (MMPI)

The Minnesota Multiphasic Personality Inventory (MMPI) has been utilized for over half a century in clinical assessment and research. [30] The original purpose of the MMPI was to assist in diagnosis of psychological disorders; however, it has also been found to be effective in personality and behavioral description.[31] The use of code types in interpretation is well researched and common in clinical practice. Code types utilize combinations of elevations, rather than interpreting, one scale at a time.[31] A two-point code type lists the highest elevation first and the second highest elevation second (e.g. 2-4). Three-point code types exist in profiles with three clinically elevated scales. This code type would be listed in a similar manner to the third highest elevation at the end (e.g. 2-4-8).The Greek adaptation of MMPI-1 is widely used in this country.[32]

MMPI is used as an indication of personality traits as well as an indication of possible psychopathology. It is based on the Diagnostic and Statistical Manual of Mental Disorders (DSM) diagnostic criteria and is also free from any psychological theoretical construct. Consequently, it serves as one of the most popular diagnostic tools in the field of Health Psychology. MMPI-1 consists of 500 true or false questions. Sample items include “I usually feel that life is worthwhile and interesting”, “Evil people are trying to influence my mind”, “I seem to hear things that other people can’t hear”.

The MMPI-1 is composed of **three validity scales:**

The “lie” (L) scale detects attempts on the part of the respondents to present themselves in a favorable light, i.e. people with high L scale scores are not willing to admit to any shortcomings and try to present themselves in a very favorable way. It should be noted that better educated people tend to score lower on the L scale, since this very scale represents in a way the naïve defensiveness of the respondent.

The infrequency (F) scale detects deviant or atypical ways of responding to test items, i.e. it is an index of test-taking attitude and is useful in detecting deviant responses.

The correction bias (K) scale detects subtle attempts to deny psychopathology on the part of respondents trying to present themselves in a favorable light or, conversely, attempts to exaggerate psychopathology and try to appear in a very unfavorable light. High scores on the K Scale are thought to be associated with an elaborate defensive approach to the test.

MMPI measures **ten major personality characteristics (scales)**. Clinical scales are designated by number and corresponding description. Each scale is composed of multiple questions that equate to a **raw score**. Raw scores are converted to **T-scores** (m=50, SD=10) and **clinical importance** is defined as a distance of more than 1.5 standard deviations.[33]

Scale 1 measures Hypochondriasis (Hs): It assesses excessive concern over body functions, somatic delusions, complaints of chronic fatigue, pain or weakness. Indeed, scale 1 measures one’s preoccupation with health and psychosomatic propensity.

Scale 2 Depression (D): It assesses poor morale, lack of hope in the future and general dissatisfaction

with life. Scale 2 evaluates one's cognitive, behavioral, emotional and physical symptoms of depression.

Scale 3 measures hysteria (Hy): It tests reaction to stress and avoidance of responsibility through development of physical symptoms. More specifically, scale 3 assesses propensity to develop physical symptoms in reaction to stress.

Scale 4 measures Psychopathic Deviation (Pd): It measures social deviation, lack of acceptance of authority and general amorality. Scale 4 evaluates one's tendency towards interpersonal conflict, rebellion, disregard of social virtues and exploitation of others.

Scale 5 measures Masculinity-Femininity (Mf): It tests masculine or feminine interests and attitudes including sexual identity; stereotypic masculine/feminine interests in work, sports, hobbies and active, vigorous, assertive personality traits. In short, scale 5 appraises a person's adherence to gender stereotypes.

Scale 6 measures Paranoia (Pa): It tests paranoid symptoms including feelings of persecution, grandiose self-concepts, ideas of reference and rigid opinions and attitudes. In point of fact, scale 6 measures one's propensity to feel misunderstood, to interpret others' actions as persecutory and socially insensitive.

Scale 7 measures Obsessive-Compulsive behavior / Psychasthenia (Pt): It tests for excessive doubts, compulsions, obsessions and unreasonable fears, self-criticism, difficulties in concentration and guilt feelings. Scale 7 assesses proneness to anxiety, worry, rumination and fearfulness in response to stress.

Scale 8 measures Schizophrenia (Sc): It tests for bizarre thoughts, peculiar perceptions, social alienation, poor familial relationships, difficulties in concentration and impulse control, disturbing questions about self-worth and self-identity and sexual difficulties. In short, scale 8 is a reality test.

Scale 9 measures HypoMania (Ma): It tests for elevated mood (with or without brief periods of depression), accelerated speech and motor activity, irritability and flight of ideas. Scale 9 appraises hyperactivity, arousal, impulsivity and grandiosity.

Finally, **scale 10 measures social introversion (Si):** It tests for withdrawal from social contacts, social introversion and retiring attitudes. Scale 10 evaluates social style including introversion/extroversion, desire for interaction and interpersonal skills.[30]

Statistical analysis

Data were analyzed using SPSS 19.0. First, descriptive statistics and normality assumption testing were explored and reported. Second, bivariate correlations among sex steroids and personality traits were computed. Third, we assessed the association of the gonadal/adrenal sex steroids with the MMPI psychometric parameters, using linear regression models. The gonadal/adrenal sex steroids served as the predictor variables and each of the MMPI psychometric parameters served as the outcome variable. The thresholds for entry into and removal from the model were set at 5% and 10%, respectively. For all regression analyses, residual scatterplots were examined to ensure that assumptions of linearity, homoscedasticity and normality were met. Mahalanobis and Cook's distances were used to identify potential outliers, which might exert undue influence on the model. Cook's distance assesses the "combined impact of the an outlier on all estimated regression coefficients". Values greater than 1 were used as a cut-off to identify extreme scores. Mahalanobis distance identifies multivariate outliers, or cases which have an unusual combination of extreme scores. A conservative probability level was used ($p<001$). The results of assumption testing and outlier examination will be discussed only when violations or outliers have been identified.

RESULTS

Descriptive Statistics and Correlations

Descriptive statistics of the gonadal/adrenal sex steroids and the MMPI subscale *T*-scores are shown in Tables 1a and 1b, respectively. Figure 1 depicts the boxplots and means of MMPI scores. Individual scores on the L, F and K scales were all below the cut-off of *T*-score = 70, generally accepted as indicating significant response bias. For the assumption of normality and $n>50$, the Kolmogorov-Smirnov test was employed. Results indicated that univariate normality was not met for all variables (see Tables 1a & 1b). Therefore, the non-parametric Spearman's correlation coefficient (rho) was used.

Table 2 depicts the descriptive statistics and inter-correlations of biochemical parameters and the MMPI's scales. Intercorrelations among gonadal/adrenal sex steroids ranged from 0.74 (LH was posi-

Table 1a. Descriptive statistics on middle luteal adrenal/gonadal sex steroids (n=59)

	Minimum	Maximum	Mean	SD	Normality (n>50)
Progesterone (ng/mL)	.30	22.30	8.89	6.35	.13
Total testosterone (ng/mL)	.10	1.35	.59	.23	.08
Free testosterone (pg/mL)	.50	5.58	2.36	1.27	.18**
FSH (mIU/ml)	.80	13.60	4.27	2.53	.14*
LH (mIU/ml)	.40	75.20	7.28	11.08	.22***
Prolactin (ng/ml)	2.30	26.00	8.52	4.40	.11
17OH-progesterone (ng/mL)	0.00	13.00	3.14	2.06	.17**
DHEAS (µg/dL)	620.00	6464.00	3001.81	1300.11	.13
D4 adrostendione (ng/ml)	.70	6.40	2.25	1.15	.17**
3 alpha-Androstendiol-G (ng/ml)	.90	14.10	5.71	2.54	.14*

Note. * p<.05; ** p<.01; *** p<.001.

Table 1b. Descriptive statistics on MMPI T-scores (N= 59)

	Minimum	Maximum	Mean	SD	Normality (n>50)
Hypochondriasis (Hs)	30.00	73.00	51.69	10.08	.07
Depression (D)	28.00	75.00	49.71	10.56	.10
Hysteria (Hy)	30.00	69.00	52.49	10.98	.12*
Psychopathic deviation (Pd)	33.00	72.00	54.25	9.78	.11
Masculinity-femininity (Mf)	24.00	67.00	48.58	9.06	.11
Paranoia (Pa)	31.00	77.00	51.68	10.96	.14**
Obsessive-compulsive/ psychasthenia (Pt)	30.00	75.00	52.37	10.75	.10
Schizophrenia (Sc)	34.00	76.00	52.79	10.51	.15**
Hypomania (Ma)	32.00	78.00	52.52	10.68	.17***
Social introversion (Si)	29.00	74.00	49.56	9.59	.09

Note. * p<.05; ** p<.01; *** p<.001.

tively correlated with FSH, p<0.01) to -0.33 (FSH was negatively correlated with progesterone, p<.01). For MMPI-1 subscales, the intercorrelations ranged from 0.80 (8-Sc was positively correlated to 7-Pt (obsessive-compulsive behavior/psychasthenia) (p<0.01) to 0.32 (9-Ma, hypomania, which was positively correlated to 7-Pt, p<0.05).

Figure 2 depicts the associations between gonadal/adrenal sex steroids and MMPI subscales. Progesterone was positively correlated to 7-Pt (obsessive-compulsive behavior/psychasthenia) (r=0.27, p<0.05); serum total testosterone was positively correlated to 6-Pa (paranoia) (r=0.27, p<0.05). Also, the metabolic product of adrenal and gonadal androgens 3alpha-diolG was positively correlated to 10-Si (social introversion) (r=0.36, p<0.05), and prolactin was correlated to 8-Sc (schizophrenia) (r=0.38, p<0.05). A trend was observed between prolactin and 4-Pd (psychopathic deviation) (r=0.26, p=0.055). No other significant correlations were revealed.

Regression diagnostics

Standard regression diagnostics were applied. Cook's distance was used for identifying influential data points. None of our cases had a Cook's distance greater than 1 and so none of the cases had an undue influence on the models. We also inspected Mahalanobis' distance (*D2*) values for potential multivariate outliers. In accordance with the recommendations of Tabachnick and Fidell,[34] the chi-square critical value for df=1 (number of independent variables) and

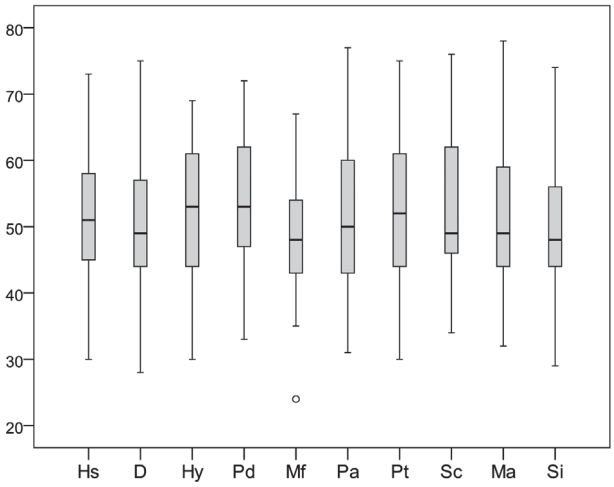

Figure 1. Boxplots of MMPI raw subscale scores for the entire sample. Hs= hypochondriasis; D= depression; Hy= hysteria; Pd= psychopathic deviation; Mf= masculinity-femininity; Pa= paranoia; Pt= obsessive-compulsive behavior/psychasthenia; Sc= schizophrenia; Ma= hypomania; Si= social introversion.

a=.01 was set to 6.64. *D2* values identified multiple outliers exceeding the critical value: 3 cases on scale 6-Pa (paranoia), 2 cases on 10-Si (social introversion) and 4 cases for 8-Sc (schizophrenia). Nevertheless, if a data point is a significant outlier on dependent variables, but its Cook distance is <1, there is no real need to delete the point since it does not have a large effect on the regression analysis. Indeed, when these cases were excluded from our models, they did not alter the general pattern of the results. Thus, we proceeded to regression models without excluding any case.

Regression analysis

Four simple linear regressions were employed and evaluated at $\alpha=0.05$. All were found to be significant or nearly significant.

In Model 1: 7% of the 7-Pt (Psychasthenia) variance was explained by *progesterone* ($R^2=0.071$, $F(1,50)=3.81$, $p=0.057$). The model is marginally insignificant. Thus, progesterone was not significantly associated with 7-Pt (Psychasthenia) ($\beta=0.27$, $p>0.05$).

In Model 2: 10% of 6-Pa (Paranoia) variance was explained by *total testosterone* ($R^2=0.10$, $F(1,57)=6.23$, $p=0.016$). It was found that total testosterone was significantly associated with Paranoia $\beta=0.32$, $t=2.50$, $p=0.016$).

In Model 3: 13% of 10-Si (Social Introversion) variance was explained by the main metabolic product of both adrenal and gonadal androgens, *3alpha-diolG* ($R^2=0.13$, $F(1,45)=6.58$, $p=0.014$). The only independent significant predictor of 10-Si (Social Introversion) was 3alpha-diolG ($\beta=0.36$, $t=2.57$, $p=0.014$).

In Model 4: 7% of 8-Sc (Schizophrenia) variance was explained by *prolactin* ($R^2=0.069$, $F(1,55)=3.98$, $p=0.051$), revealing a marginally significant regression coefficient for prolactin ($\beta=0.26$, $t=1.99$, $p=0.051$).

DISCUSSION

Over the past four decades a great number of reports have been published showing several associations between circulating adrenal and gonadal sex steroids in pre- and post-menopausal women and various psychometric characteristics. However, no published report has examined the connection between a complete profile of circulating adrenal and gonadal sex steroids and psychological parameters in young, healthy, professional and normally ovulating women with no apparent medical problems. The aim of the present study was to determine the associations, if any, between the circulating levels of gonadal and adrenal sex steroids in the mid luteal phase (21st day of a normal, MC) of young professional women and psychometric parameters as assessed by the MMPI. We have found several interesting associations and we compare our findings with the extensive bibliography on this subject.

Androgens: It is usually very difficult to document a robust association between circulating androgen levels and behavioral traits not only because of the well-known covariance problem in biological and behavioral measurements but also because activation of testosterone usually takes place within the target tissue by being converted to dihydro-testosterone, little of which escapes into systemic circulation where it may be used as a marker of bioactive testosterone. Indeed dihydro-testosterone, a reliable marker of testosterone activity, is not easily measurable. However, its metabolic product, 3alpha-diolG, has been shown to be a sensitive index of androgenic activity, unsurpassed by parallel measurements of all other androgens including serum total or free testoster-

Table 2. Intercorrelations of biochemical parameters and MMPI's subscales (n= 59)

	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20
1. Prog	--																			
2. 3a- ADG	-0.11	--																		
3.DHEAS	-0.03	0.19	--																	
4.Ttesto	0.04	0.14	0.45**	--																
5.Ftesto	-0.06	0.38**	0,48**	0.50**	--															
6.D4A	-0.21	0.37*	0.28	0.15	0.28	--														
7. 17 0 HP	0.62**	0.05	-0.01	-0.09	0.03	-0.04	--													
8. FSH	-0.33**	0.20	0.14	0.10	0.26*	0.07	-0.18	--												
9.LH	-0.25	0.25	0.10	0.20	0.29*	0.16	-0.14	0.74**	--											
10.PRL	-0.26	-0.09	0.16	0.13	0.03	0.41**	0.07	-0.12	-0.07	--										
11. Hs	-0.06	-0.05	-0.01	0.03	-0.19	-0.08	0.02	-0.12	-0.14	-	--									
12. D	-0.01	0.01	-0.01	0.00	-0.01	0.04	-0.02	-013	-0.20	0.09	0.51**	--								
13. Hy	-0.03	-0.20	-0.07	-0.06	-0.13	-0.13	0.02	-0.21	-0.20	0.02	0.76**	0.54**	--							
14.Pd	-0.12	0.01	0.05	0.11	0.07	0.09	0.05	-0.16	-0.05	0.26*	0.45**	0.46**	0.46**	--						
15. MF	0.03	0.08	-0.08	-0.02	0.03	0.09	0.18	-0.07	-0.03	-0.04	0.17	-	0.04	0.14	--					
16. Pa	0.11	0.14	0.07	0.27*	-0.01	-0.10	0.07	-0.09	0.03	0.06	0.42**	0.51**	0.41**	0.48**	0.06	--				
17. Pt	0.27*	-0.02	0.09	0.08	0.06	-0.02	0.17	-0.21	-0.17	0.27*	0.57**	0.73**	0.53**	0.55**	0.11	0.67**	--			
18.Sc	0.14	-0.04	0.15	0.19	0.05	-0.02	0.08	-0.10	-0.01	0.38*	0.52**	0.57**	0.49**	0.68**	0.20	0.66**	0.80**	--		
19. Ma	0.13	0.18	-0.01	0.21	0.02	-0.04	-0.05	-0.09	-0.04	0.23	0.15	-0.01	0.08	0.11	0.14	0.43**	0.32*	0.45**	--	
20. Si	0.05	0.36*	0.13	0.10	0.09	0.11	--	--	0.12	0.20	0.12	0.47**	-0.05	0.20	-0.08	0.33*	0.37**	0.38**	0.02	--

one, DHEA or DHEA-S.[35] In our study, the metabolic product of activated adrenal and gonadal androgens, 3alpha-diolG, was modestly but significantly associated with social introversion (10-SI) ($r=0.36$, $p<0.05$), independently accounting for 13% of its variation across participants ($R^2=0.13$, $F(1,45)=6.58$, $p=0.014$). In a study of sixty-nine pre-menopausal hirsute women assessed by the General Health Questionnaire and the Profile of Mood States (POMS) to evaluate psychological morbidity, poor social adjustment, higher levels of neuroticism and social introversion and avoidance of some social situations was observed in a quarter of the hirsute women examined.[36] The authors were unable to document any association between behavioral parameters and the severity of hirsutism or testosterone levels. The results suggested that a proportion of women with hirsutism experienced psychological and social difficulties from factors other than their dermatological-cosmetic status and testosterone levels.

Total testosterone was significantly associated with the paranoia subscale (6-Pa) ($r=0.27$, $p<0.05$). Multiple regression analyses indicated that 10% of the variability in paranoia scores could be independently explained by total testosterone levels ($R^2=0.10$, $F(1,57)=6.23$, $p=0.016$). Most of the published literature documenting an association between androgens and paranoid ideation is based on studies associating consumption

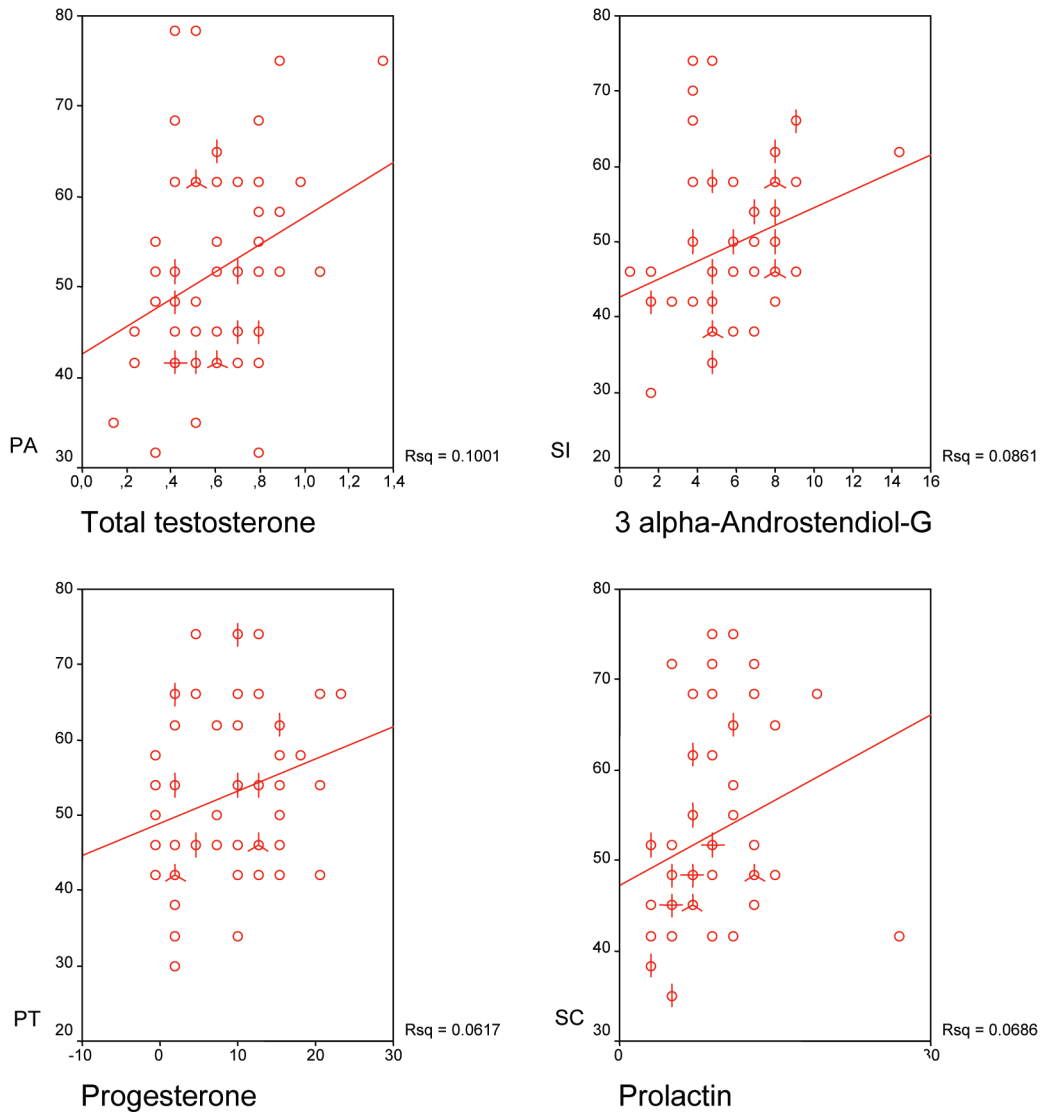

Figure 2. Scatter-plots showing significant (top) or trend for significant (bottom) correlations between sex steroids and MMPI psychometric variables.

of large quantities of anabolic androgenic steroids with paranoid ideation, depression, anxiety, obsessive compulsiveness behavior, etc.[37-41] In women, not consuming anabolic androgenic steroids, no correlation could be established between endogenous serum androgens and clinical measures of psychopathology either in normal or in hirsute persons.[26] To our knowledge, ours is the first report associating the mild elevations of endogenous androgens in the mid luteal phase of normally menstruating young women with paranoid ideation, indicating that even these mild and physiologically normal elevations of endogenous androgens may indeed affect human behavior.

It is also of interest that we were unable to detect any association between the circulating androgens, in the mid-luteal phase of our population of normally menstruating young females, and depression, although this appears to be a well-documented association in older peri- or post-menopausal women[15,42] as well as in women with polycystic ovarian syndrome (a classical hyper-androgenic state) where free testosterone levels were found to correlate with depression and anxiety.[14] Similarly, in hirsute women (serum testosterone high enough to be clinically evident as hirsutism), its levels correlated significantly with depression.[12] Interestingly, the higher incidence of depression in

facially hirsute women correlated better with circulating testosterone rather than with the degree of facial hirsutism itself.[11,13] Again, in a community-based baseline cohort of 2961 women aged 42-52yr from the Study of Women's Health Across the Nation, the self-reported scale of depressive symptomatology (Center for Epidemiologic Studies Depression Scale score) correlated positively with serum testosterone.[15] Indeed, it has been suggested that serum testosterone may predict clinical depression in pre-menopausal women.[43] Interestingly, testosterone administration has been shown to improve mood and sense of well-being in pre-menopausal women with low libido and low testosterone.[44] However, another study has found that the addition of testosterone to estrogen replacement therapy in oophorectomized women enhanced the effect of estrogens on sexuality but did not appear to affect the sense of well-being and self-esteem.[45] Furthermore, testosterone and DHEA-S in older women did not correlate with depression.[46] Similarly, in an older study measuring 17-ketosteroids and testosterone in women without chemical or laboratory evidence of hyper-androgenism, no correlation was found between androgens and specific personality traits, including depression.[25] We were also unable to document in our young population any correlation between the weak adrenal androgens DHEA and DHEA-S and depression in contrast to several published reports.[23,24,47] It should be noted that there is rich but still controversial literature on the effects of DHEA and DHEA-S on cognitive skills in older individuals.[48]

Finally, we were unable to detect any association between the circulating androgens and scores on the masculinity/femininity scale. We hypothesize that failure to corroborate previous findings on the relation between testosterone levels and aggression may be due to either the characteristics of our population (it was composed of individuals with no clinical or laboratory evidence of hyper-androgenism including no hirsutism, menstrual irregularities or anovulatory cycles) or it may be due to limitations of the MMPI questionnaire since this is not a sensitive tool in assessing aggression compared to other questionnaires specifically designed to assess it. Nevertheless, in a study using the MMPI questionnaire, a positive correlation has been found between the "weak" adrenal androgen DHEA-S and traits indicative of an expansive and egocentric personality profile.[22] However, studies using different questionnaires have documented such correlations. Indeed, in female students high salivary testosterone correlated with an action-oriented profile assessed by the Baucom's Masculinity and Femininity questionnaire.[16] Similarly, high serum testosterone has been associated with higher dominance scores in young women.[17] A positive correlation between testosterone, strong personality characteristics and professional rank has also been shown in young Saudi women.[19] It is of interest that high circulating testosterone has been associated with lower scores of maternal personality (evaluated by the Bem Sex Role Inventory) and reproductive ambition, a finding suggesting that maternal tendencies appeared to be influenced by circulating testosterone.[18,21]

Progesterone: Our data suggest a marginally significant association between progesterone and scores on the 7-Pt (obsessive/compulsive/psychasthenia) scale ($r=0.27$, $p<0.05$). However, only 7% of the 7-Pt (Psychasthenia) variance was explained by progesterone ($R^2=0.071$, $F(1,50)=3.81$, $p=0.057$). It is of interest that reports on unusual cleaning behavior during the luteal phase of normally menstruating young women have been published, suggesting an association between progesterone and obsessive/compulsive disorders.[1] Our data tend to support these reports, although the above authors did not actually measure progesterone in their samples. They assumed high progesterone because of the timing of blood-letting, i.e. in the middle of the luteal phase. However, we were definitely unable to document any association between levels of serum progesterone and depression, although several published studies have reported the surfacing of negative mood during the second part of the MC when serum progesterone levels are the highest.[6] However, pharmacological administration of progesterone to ovariectomized rats has been shown to exert an anti-depressant effect.[49] Furthermore, in humans, the sudden decline of progesterone following delivery has been implicated in post-menopausal depression, the so-called postpartum blues.[7] Our inability to find any statistical correlation (positive or negative) between serum levels of progesterone and depression cannot be attributed to low sensitivity of our questionnaire since a significant correlation was evident between serum androgens and depression. Furthermore, a possible anti-depressant effect of

progesterone did not completely mask the depression-augmenting effect of androgens, although it may well have decreased its magnitude.

Limitations of our study: Because of the relatively small number of subjects in this study and the highly selected nature of the women involved in it, our results should be interpreted with caution and viewed as a probable guide to emerging behavioral patterns. Conclusive confirmation of these patterns should be tested in a larger and possibly more heterogeneous/representative sample.

In conclusion, we have found in the mid-luteal phase of our population composed of young, professional, normally menstruating, healthy women that the circulating total testosterone was associated with paranoia, the metabolic product of activated testosterone 3alpha-diolG was significantly associated with social introversion and the progesterone correlated to obsessive-compulsive behavior. Contrary to published reports, we were unable to document any association between circulating androgens and the "masculinity/femininity" scale or depression, nor between progesterone levels and depression.

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