Age and Training Intensity Differently Affect Male Runners' Endocrine and Sexual Parameters

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Abstract

Physical activity is widely recognized to improve health and its inclusion in daily life at all ages is highly recommended. Gonadal hormones are known to be affected by physical activity. The exercise-induced effects on male runners of different ages were investigated by dividing 31 runners by age (Young, Y, 30–55 years; Old, O, 56–70 years) and amount of training (Light, L, <50 km/week; Heavy, H, 50 or more km/week). To test the somatic, sexual, and psychological health aspects, the Aging Male's Symptoms Scale (AMS) and the International Index of Erectile Function-6 (IIEF-6) questionnaires were administered and blood samples were drawn for adrenocorticotropic hormone, testosterone (Total-TT), free testosterone (Free-T), cortisol (C), dihydrotestosterone (DHT), estradiol, and sex hormone-binding globulin determinations. Clinical evaluations and questionnaire results showed the presence in all groups of some subclinical symptoms and "Light" dysfunctions. TT in the old-heavy (OH) group was significantly lower than in the OL group (2.38 ± 0.18 ng/mL vs. 3.36 ± 0.44 ng/ml, $P = 0.05$). The TT/DHT ratio was significantly higher in YH than in OH (3.64 ± 0.16 vs. 2.92 ± 0.23, $P < 0.05$). TT was positively correlated with AMS sexual subscale and *negatively* correlated with IIEF-6. Physical activity can significantly affect andrological health and testosterone levels in runners at all ages. Thus, due to the important testosterone-mediated vital functions in men, the evaluation of these parameters would be indicated in old as well as in young subjects.

Keywords: Hormones, runner, sexual functions, testosterone

Introduction

Regular physical activity leads to physiological adaptations, with structural and functional adjustments present at the somatic, endocrine, and immune levels. Specifically, endocrine changes are known to have an important effect on reproductive functions, as commonly observed in female athletes.[1-4]

In males, clinical signs such as testicular hypotrophy, libido disruption, and erectile dysfunction were reported in male athletes performing the high-intensity activity.[5,6] Hackney *et al*. demonstrated how regular endurance training at high intensities and great durations was significantly connected with a decreased libido in men.[7] In addition, exercise-induced suppression of testosterone (T) was associated with impairment of the hypothalamic-pituitary-gonadal (HPG) axis during exercise.[8] Karkoulias *et al*. demonstrated that both hypothalamic and testicular functions were affected during and immediately after a marathon in nonelite runners.[6] Instead, Kumagai *et al*. suggested that regular aerobic exercise is an effective strategy to improve aging-induced sexual disorder in men[2] and Cook *et al*. established that total testosterone (TT), free testosterone (Free-T) and dihydrotestosterone (DHT) concentrations were higher during a high-volume loading trial than in the pretrial period in a study of 28 cyclists of both sexes.[9] However, only a few studies have investigated how the duration and intensity of training can lead to physiological adaptations in runners.[5,10]

After the 50th year of age, T secretion by the testes physiologically decreases by 50% and the circadian rhythm

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of T production is lost, mostly due to alterations in the HPG axis that regulates T production.[3,11] Consequently, several reproductive and nonreproductive functions can be affected. In particular, the importance of T in cognitive and metabolic functions is clear,[12,13] as is the effect of T on aspects of physical performance such as skeletal muscle mass,[14] muscle strength, fat-free mass, physical function, bone mineral density, and risk of fracture.[15,16]

The aim of this study was to investigate in male runners the effect of the training volume and age on hormonal values and sexual parameters determined with dedicated questionnaires. A preliminary report was presented at the Italian Society of Physiology congress.[17]

Materials and Methods

The experimental protocol adhered to the principles of the Declaration of Helsinki; written informed consent was obtained from all runners before their enrolment in the study. Blood samples for hormonal detection were collected from each runner from 8 to 10 am of the testing day. Moreover, accurate physical and andrological examinations were carried out. Two validated questionnaires (Aging Male's Symptoms Scale [AMS]; International Index of Erectile Function-6 [IIEF-6]) were used to evaluate male sexual functions.

Subjects

Male runners were asked to participate in the study. Inclusion criteria were: age 30–70 years old; no metabolic or chronic pathologies, signing of the informed consent form. Runners were asked to report:

- The years of sporting activity practiced
- Number of trainings per week
- The time spent running per training
- The time spent running per week
- The kilometers run per week
- The kilometers run in the previous month
- The kilometers run in the previous 3 days.

Runners were then divided by age (Young, Y, 30–55 years; Old, O, 56–70 years) and amount of training (Light, L, <50 km/week; Heavy, H, 50, or more km/week). Thus, as shown in [Table 1], runners were categorized into the following groups:

- Young-Light (YL; 30-55 years; <50 km/week)
- Young-Heavy (YH; 30-55 years; ≥50 km/week)
- Old-Light (OL; 56-70 years; <50 km/week)
- Old-Heavy (OH; 56-70 years; ≥50 km/week).

Questionnaires

Aging Male's Symptoms Scale – assesses the severity of Aging Male's Symptoms.[18] It includes 17 questions divided into 3 subscales to investigate somatic, psychological, and sexual symptoms. Each question has to be answered with a score from 1 to 5. The lower the amount, the better the condition.[19,20]

International Index of Erectile Function-6 – a multidimensional self-report instrument consisting of 6 items evaluating erectile dysfunction.[21] Each question has to be answered with a score from 0 to 5. The lower the amount, the higher the dysfunction.[22]

Blood samples analysis

All subjects had fasted for at least 12 h before the blood sampling. In the testing procedure, 5 + 5 mL of blood were drawn from an antecubital vein and collected in two vacutainer tubes (Becton Dickinson and Company, UK), one heparinized to obtain plasma and one empty to obtain serum. Blood samples were treated by centrifugation (5702R, Eppendorf, Germany) at 3000 g for 10 min at 4°C. Plasma (only for adrenocorticotropic hormone, ACTH) and serum aliquots were then stored at -80°C till hormonal determination.

TT, Free-T, DHT, estradiol (E2), and cortisol (C) were determined by radioimmunoassay (RIA). Immunoradiometric assay (IRMA) was performed to determine ACTH and sex hormone-binding globulin (SHBG) values.

TT and C were measured by RIA using a kit from RADIM (Pomezia, Italy). For TT, the cross-reactivity of the antiserum coated in the tubes was 5.6% for DHT, 1.6% for androstenedione, and lower than 0.1% for androstenediol, SHBG, estrone, DHEAS, and E2. The lower limit of quantitation of TT measured by this assay was 0.017 ng/mL. The intra- and inter-assay coefficients were 1.5% and 7.8%, respectively, at the normal adult male range: 3.5–8.5 ng/mL. For C, the present method has not shown cross-reaction with the following steroids: E2, T, prednisone, cortisone, corticosterone, deoxycorticosterone, and 11-deoxycortisol. The lower limit of quantitation of serum C measured by this assay was 0.9 μg/L. The intra- and inter-assay coefficients were 4.9% and 7.9%, respectively, at the normal adult male range: 50–250 μg/L.

Table 1: Detailed description of demographic and training data divided by age and training level

	Age (years)	Sport practice (years)	Number of trainings/week	Time training (min)	H/week	Km/week	Km in the last month	Km in the last 3 days
YL (*n*=8)	48.1±2.3	22.1±3.8	3.6±0.6	65.6±6.9	4.4±0.6	30.0±3.4	98.1±15.2	15.0±2.2
YH (*n*=7)	43.7±2.7	17.1±4.9	4.6±0.5	106.4±17.9	7.1±1.2	85.7±16.7	277.1±40.8	33.1±9.4
OL (*n*=9)	65.8±1.5	25.4±6.3	3.9±0.5	83.6±16.6	5.3±1.0	30.0±3.4	94.4±14.7	12.9±1.4
OH (*n*=7)	60.7±1.1	28.0±3.3	4.9±0.3	88.6±12.6	6.7±1.0	76.4±12.8	220.0±47.9	27.6±4.1

Y (Young, 30-55 years), O (Old, 56-70 years), L (Light physical activity, km/week <50), H (Heavy physical activity, km/week ≥50), H/week (Hours/week). *n*=31. Values are reported as mean±SEM. SEM: Standard error of the mean

Free-T, DHT, E2 were measured by RIA using a kit from Diagnostic Systems Laboratories (Webster, TX, USA). For Free-T, the cross-reactivity of the antiserum coated in the tubes was 0.35% for 19-nor testosterone, 0.21% for 17 alpha-methyltestosterone, 0.13% for 11-oxo-testosterone, and non-detectable reactivity for DHT, DHEA, DHEA-S, progesterone, E2, corticosterone, and other androgens. The lower limit of quantitation of Free-T measured by this assay was 0.18 pg/mL. The intra- and inter-assay coefficients were 4.5% and 7.9%, respectively, at the normal adult male range: 14.7–32.7 pg/mL. For DHT, the cross-reactivity of the antiserum coated in the tubes was 3.3% for androstanol glucuronide, 0.6% for T, 0.03% for androstanol, and no reactivity for androstenedione, E2, androsterone glucuronide, dehydroepiandrosterone, cortisol, deoxycortisol, 17 alpha-OH progesterone, and progesterone. The lower limit of quantitation of DHT measured by this assay was 4 pg/mL. The intra- and inter-assay coefficients were 3.7% and 6.9%, respectively, at the normal adult male range: 250–750 pg/mL. For E2, the cross-reactivity of the antiserum coated in the tubes was 2.4% for estrone, 0.21% for 17 alpha-E2 and 16 keto-E2, 0.64% for estriol. The lower limit of quantitation of E2 measured by this assay was 2.2 pg/mL. The intra- and inter-assay coefficients were 5.3% and 8.1%, respectively, at the normal adult male range: 10.0–25.1 pg/mL.

ACTH was measured in plasma by IRMA using a kit from RADIM (Pomezia, Italy). The present method has not shown cross-reaction with the following synthetic peptides: ACTH (18–39), ACTH (1–10), ACTH (1–24), α-MSH, β-MSH, β-endorphin. The lower limit of quantitation of plasma ACTH measured by this assay was 1.0 pg/mL. The intra- and inter-assay coefficients were 7.8% and 11.8%, respectively, at the normal adult male range: 5–77 pg/mL.

SHBG was measured by IRMA using a kit from Diagnostic Systems Laboratories (DSL, Webster, TX, USA). Concerning the specificity, no human serum protein is known to cross-react with the antibodies employed in the DSL SHBG IRMA system. The lower limit of quantitation of serum SHBG measured by this assay was 3 nmol/L. The intra- and inter-assay coefficients were 2.7% and 10.2%, respectively, at the normal adult male range: 28–94 nmol/L.

Statistical analysis

After a normality check (Shapiro-Wilk test), all normally distributed data were subjected to a two-way ANOVA with the factors Age (2 levels: Young, Old) and Training (2 levels: Light, Heavy). Data not normally distributed (SHBG, TT, ACTH, C, Free-T, TT/C, AMS sexual subscale, and IIEF-6) were subjected to the Kolmogorov–Smirnov test. Partial correlation and Spearman rank were applied to evaluate correlations between parameters. Significance was accepted at $P < 0.05$. *Post hoc* analysis was carried out using Fisher's least significant difference test. Statistica® software was used for the analysis. Data are reported as mean ± standard error of the mean.

Results

Forty subjects agreed to participate in the study and 31 completed all the experimental procedures. They were divided into the following groups: YL: n = 8, YH: n = 7, OL: n = 9, OH: n = 7. Detailed demographic characteristics are reported in [Tables 1 and 2].

The clinical evaluation resulted in: Old, 1 case of testicular hypotrophy, 3 cases of dysuria and nocturia, 2 cases of decreased libido, 1 case of unstable erection; Young, 1 case of testicular hypotrophy, 2 cases of decreased libido, 2 cases of the altered prostate gland.

As reported in [Table 1], running activity had been carried out by the different groups for several years, the mean being 22.9 ± 2.4 years; the number of trainings per week ranged from 1 to 7, the time spent per training from 30 to 180 min, the hours training per week from 1 to 14, the number of kilometers per week from 15 to 150, the number of kilometers in the previous month from 30 to 500 and the number of kilometers in the previous 3 days from 6 to 80.

Questionnaires

Scores from the questionnaires are reported in [Table 3]. In the AMS, 19/31 subjects reported some kind of dysfunction: 13 reported Light dysfunction (3YL, 2YH, 4OL, 4OH) and 6 Moderate dysfunction (1YL, 2YH, 2OL, 1OH), with the highest (worst) condition being present in the YH group. No significant differences were found among the groups. In the IIEF-6, 10/31 subjects reported some kind of dysfunction: 7 reported Light dysfunctions (1YL, 2YH, 2OL, 1OH), 2 subjects Moderate (2OL), and 1 Severe (OH).

Exercise parameters were correlated with questionnaire data [Table 4]. In particular, time training per week and hours/week were correlated with AMS psychological subscale ($n = 27$, $r = 0.41$, $P < 0.05$ and n = 28, $r = 0.37$, $P < 0.05$, respectively), km/week and km in the last month were correlated with AMS psychological and somatic subscales ($n = 28$, $r = 0.49$ and $r = 0.50$, $P < 0.01$ and $r = 0.44$ and $r = 0.45$, $P < 0.05$, respectively). In all cases since higher AMS values mean a worse condition, the positive correlations between AMS and training levels suggest a detrimental effect of training on male psychological and somatic functions. In contrast, "km in the last 3 days" was negatively correlated with AMS sexual subscale ($n = 28$, $r = -0.40$, $P < 0.05$), indicating a beneficial effect of training on male sexual function. This result is supported by the km/week and IIEF-6 values that were positively correlated ($n = 27$, $r = 0.39$, $P < 0.05$); in this case since higher IIEF values mean a good condition, the positive correlation seems to indicate a beneficial effect of training on erectile function.

Hormones

As evident from the single values per subject reported in [Table 2] and the mean values reported in [Figure 1], all groups/subjects showed TT and Free-T values at the lower normal limit. The Kolmogorov–Smirnov test applied to TT

Table 2: Detailed description of participants

S	Age	Age range	Physical activity	Km/week	H/week	TT (ng/ml)	Cortisol (μg/L)	SHBG (nmol/L)	AMS tot	IIEF-6
S01	54	Y	L	35	5	1.8	94.3	54.1	40	18
S02	68	O	L	25	3	2.7	104.6	63.4	28	17
S03	33	Y	H	50	7	4.1	124.1	59.7		
S04	69	O	L	40	3	2.3	163.8	64.7	30	30
S05	38	Y	H	100	6	3.4	102.4	49.8	34	26
S06	47	Y	H	150	7	1.4	136.7	43.3	32	29
S07	67	O	L	15	12	3.8	206.3	78.7	33	22
S08	52	Y	L	40	3	2.9	196.7	86.3	34	
S09	59	O	H	70	6	2.0	296.0		27	29
S10	38	Y	L	20	6	2.1	157.8	51.0	18	30
S11	59	O	H	80	12	2.0	109.3	60.0	28	29
S12	58	O	H	150	8	2.2	120.1	84.5	36	30
S13	66	O	L	40	6	2.9	99.2	46.7	38	13
S14	58	O	L	40	6	2.6	108.4	45.2	29	30
S15	63	O	H	60	5	2.7	141.6	75.7	37	23
S16	65	O	H	65	5	3.3	107.8	53.9	25	30
S17	45	Y	L	20	6	3.3	217.1	118.1	18	
S18	58	O	H	60	5	2.3	119.5	43.8	36	20
S19	60	O	L	30	6	6.6	137.8	27.1	40	11
S20	42	Y	H	50	6	3.8	79.7	68.1	23	29
S21	48	Y	H	140	14	2.4	133.2	42.9	19	35
S22	67	O	L	20	3	3.0	241.7	155.5	23	29
S23	72	O	L	20	3	3.6	155.5	74.3		20
S24	63	O	H	50	6	2.1	185.9	46.8	23	32
S25	52	Y	L	20	1	3.1	236.8	47.4	25	27
S26	43	Y	H	60	6	3.1	197.2	48.6	19	30
S27	55	Y	L	30	5	2.3	137.3	55.6	26	29
S28	55	Y	H	50	4	3.2	231.1	70.0	44	17
S29	65	O	L	40	6	2.8	154.3	78.8		
S30	45	Y	L	45	4	4.3	137.7	61.2	30	30
S31	42	Y	L	30	5	2.9	181.9	60.8	35	26

S (Subjects), Y (Young, 30-55 years), O (Old, 56-70 years), L (Light physical activity, km/week <50), H (Heavy physical activity, km/week ≥50), H/week (Hours/week), TT (Total Testosterone), SHBG (Sex Hormone-Binding Globulin), AMS tot (Aging Male's Symptoms Scale total), IIEF-6 (International Index of Erectile Function-6). N=31

Table 3: Andrological evaluation

Questionnaires	Age range (years)	Light (km/ week)	Heavy (km/ week)	Reference values (severity)
AMS (*n*=28)	Y	28.3±2.8	28.5±4.1	17-26: No
	O	31.6±2.2	30.3±2.2	27-36: Light
				37-49: Moderate
				>50: Severe
IIEF-6 (*n*=27)	Y	26.7±1.9	27.6±2.4	26-30: No
	O	21.5±2.7	27.6±1.6	17-25: Light
				11-16: Moderate
				<10: Severe

Y (Young, 30-55 years), O (Old, 56-70 years); AMS: Aging Male's Symptoms Scale, IIEF-6: International Index of Erectile Function-6. Light: <50 km/week, Heavy: ≥50 km/week. Values are reported as mean±SEM. SEM: Standard error of the mean

revealed significant variations between OH and OL ($P < 0.05$), due to lower TT levels in OH than in OL (2.38 ± 0.18 ng/mL vs. 3.36 ± 0.44 ng/mL) [Figure 1]. Instead, a nonsignificant difference was observed between YL and YH (2.84 ± 0.28 ng/mL vs. 3.05 ± 0.35 ng/mL; $P > 0.05$).

Free-T, E2, DHT, C, ACTH, and SHBG did not show significant differences among groups [Figures 1 and 2]. ANOVA applied to the TT/DHT ratio showed a significant age x Training interaction ($F[1,26] = 5.2$, $P < 0.05$) [Figure 3a], due to the higher levels in YH than in OH ($P < 0.05$). No significant effects were observed for TT/C and TT/E [Figure 3b and c].

As expected, TT was positively correlated with Free-T ($n = 30$, $r = 0.66$; $P < 0.001$), DHT ($n = 30$, $r = 0.83$; $P < 0.001$) and E2 ($n = 23$, $r = 0.54$; $P < 0.01$) [Table 5]. Correlations between hormonal levels and outcomes from AMS/IIEF-6 are reported in [Table 6]. In detail, TT and E2 were positively correlated with AMS sexual subscale, while TT, DHT, and E2 were *negatively* correlated with IIEF-6 values. Thus, in both cases when hormonal levels are higher the AMS/IIEF-6 scores worsen, suggesting a lack of body adaptation to the physical activity levels experienced. Moreover, ACTH, the stress

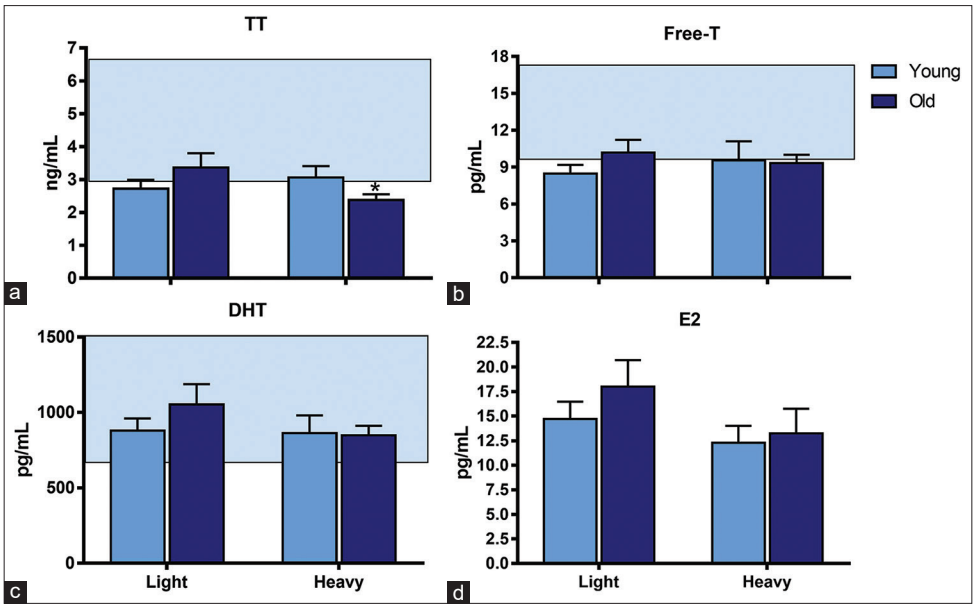

Figure 1: For both light (<50 km/week) and heavy (≥50 km/week) training, (a) TT, (b) Free-T, (c) DHT and (d) E2 are reported. Comparisons between young (30–55 years) and old (56-70 years) men are outlined as mean and standard error (vertical bars). Rectangle in the background defines normal values. Abbreviations: TT: Total testosterone, Free-T: Free testosterone, DHT: Dihydrotestosterone, E2: Estradiol. Significantly different: *$P < 0.05$, OH versus OL.

Table 4: Correlations between questionnaires and training data

	AMS psychological	AMS somatic	AMS sexual	AMS total	IIEF-6
Sport practice	NS	NS	NS	NS	NS
Number of trainings/week	NS	NS	NS	NS	NS
Time training	r=0.41 P<0.05 (n=27)	NS	NS	NS	NS
H/week	r=0.37 P<0.05 (n=28)	NS	NS	NS	NS
Km/week	r=0.49 P<0.01 (n=28)	r=0.50 P<0.01 (n=28)	NS	NS	r=0.39 P<0.05 (n=27)
Km in the last month	r=0.44 P<0.05 (n=28)	r=0.45 *P<0.05 (n=28)*	NS	NS	NS
Km in the last three days	NS	NS	r=−0.40 P<0.05 (n=28)	NS	NS

AMS: Aging Male's Symptoms Scale, IIEF-6: International Index of Erectile Function-6, NS: No significance, r: Linear correlation coefficient, *P*: Statistical significance, *P*-value. Correlations are significant at P<0.05

Table 5: Correlations between hormones and hormones ratio

	TT	TT/E2	TT/C	TT/DHT
TT (n=31)		NS	r=0.74 P<0.001	NS
Free-T (n=30)	r=0.66 P<0.001	NS	r=0.62 P<0.001	NS
DHT (n=30)	r=0.83 P<0.001	NS	r=0.47 P=0.01	r=−039 P<0.05
E2 (n=23)	r=0.54 P<0.01	r=−0.59 P<0.01	r=0.47 P<0.05	NS

TT: Total testosterone, Free-T: Free testosterone, DHT: Dihydrotestosterone, E2: Estradiol, C: Cortisol, NS: No significance, r: Linear correlation coefficient, *P*: Statistical significance, *P*-value. Correlations are significant at P<0.05

hormone, was negatively correlated with AMS total and in this case, since lower AMS total values mean a better condition, the negative correlations indicate a better condition in those with a higher responsive hypothalamic-pituitary-adrenal axis (HPA) (i.e., with higher ACTH).

As reported in [Table 7], DHT was negatively correlated with km/week (n = 30, r = −0.48, P < 0.01), km in the last month (n = 30, r = −0.41, P < 0.05) and km in the last 3 days (n = 30, r = −0.46, P < 0.01); E2 was negatively correlated with km/week (n = 23, r = −0.44, P < 0.05) and km in the last month (n = 23, r = −0.43, P < 0.05) and TT was negatively correlated with km in the last 3 days (n = 31, r = −0.41, P < 0.05).

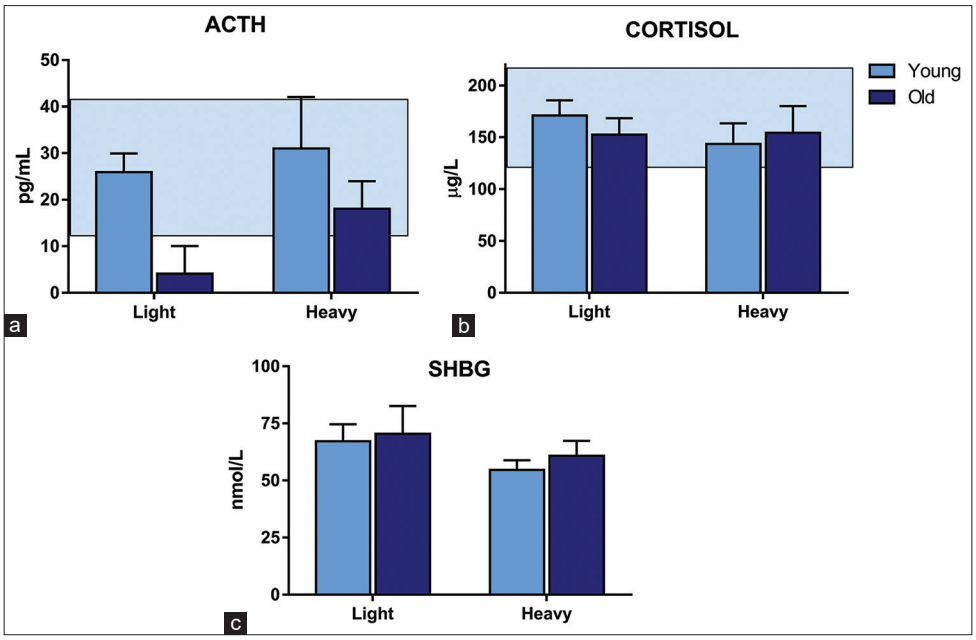

Figure 2: For both light (<50 km/week) and heavy (≥50 km/week) training, (a) ACTH, (b) cortisol and (c) SHBG are reported. Comparisons between young (30–55 years) and old (56–70 years) men are outlined as mean and standard error (vertical bars). Rectangle in the background defines normal values. Abbreviations: ACTH: Adrenocorticotropic hormone, SHBG: Sex hormone-binding globulin.

Table 6: Correlations between questionnaire data and hormonal values

	AMS psychological	AMS somatic	AMS sexual	AMS total	IIEF-6
TT	NS	NS	r=0.38 P<0.05 (n=28)	NS	r=−0.44 P<0.05 (n=27)
Free-T	NS	NS	NS	NS	NS
DHT	NS	NS	NS	NS	r=−0.43 P<0.05 (n=26)
E2	NS	NS	r=0.54 P<0.01 (n=22)	NS	r=−0.45 P<0.05 (n=20)
ACTH	NS	NS	NS	r=−0.50 P<0.01 (n=28)	NS

TT: Total testosterone, Free-T: Free testosterone, DHT: Dihydrotestosterone, E2: Estradiol, ACTH: Adrenocorticotropic hormone, AMS: Aging Male's Symptoms Scale, IIEF-6: International Index of Erectile Function-6, NS: No significance, r: Linear correlation coefficient, *P*: Statistical significance, *P*-value. Correlations are significant at P<0.05

Discussion

The main result of the present study is the training-induced effect on the health of male runners of different ages; indeed endocrinopathies and andrological dysfunctions were found independently of the age.

Hypogonadism occurs when the gonads do not secrete hormones appropriately with regard to the sex, age, day, and fertility period.[23,24] In men, aging and other factors may lead to a testosterone decrease.[25] For instance, hypogonadism is known in patients taking drugs to treat chronic pain,[26-29] obesity,[30] depressive disorder,[31] but also in healthy athletic subjects. Indeed, while exercising, the human body encounters physical and psychological conditions influencing the release and modulation of steroid hormones, especially in high-intensity training.[32-34] Many studies have reported that the type and duration of exercise and environmental conditions can influence testosterone plasma levels.[35-37] For instance, low T levels were found in athletes involved in endurance performances.[5,8,15,34,38-40] In contrast, Hayes and colleagues demonstrated that a 6-week period of moderate aerobic exercise increased TT in sedentary older males.[41] The same research group showed that a combination of exercise preconditioning (required in sedentary cohorts) and high-intensity interval training was a sufficient stimulus to improve Free-T in lifelong sedentary aging men.[41] Duclos *et al*.[42] found increased Free-T after intense exercise regardless of duration, while low-intensity exercise did not affect Free-T and luteinizing hormone (LH). Finally, combined sprint and resistance in a training protocol of 13 weeks increased basal serum TT and Free-T in the middle-aged trained group, while no changes were observed in the young or control groups, which canceled the age-effect on anabolic hormones posttraining.[43]

Table 7: Correlations between hormonal levels and training data

	TT	Free-T	DHT	E2	C	SHBG	ACTH
Sport practice	NS	NS	NS	NS	NS	NS	NS
Number of trainings/week	NS	NS	NS	NS	NS	NS	NS
Time training	NS	NS	NS	NS	NS	NS	NS
H/week	NS	NS	NS	NS	NS	NS	NS
Km/week	NS	NS	r=−0.48 P<0.01 (n=30)	NS	r=−0.44 P<0.05 (n=23)	NS	NS
Km in the last month	NS	NS	r=−0.41 P<0.05 (n=30)	NS	r=−0.43 P<0.05 (n=23)	NS	NS
Km in the last 3 days	NS	NS	r=−0.46 P<0.01 (n=30)	NS	ns	r=−0.41 P<0.05 (n=31)	NS

TT: Total testosterone, Free-T: Free testosterone, DHT: Dihydrotestosterone, E2: Estradiol, C: Cortisol, SHBG: Sex hormone-binding globulin, ACTH: Adrenocorticotropic hormone, NS: No significance, r: Linear correlation coefficient, *P*: Statistical significance, *P*-value. Correlations are significant at *P*<0.05

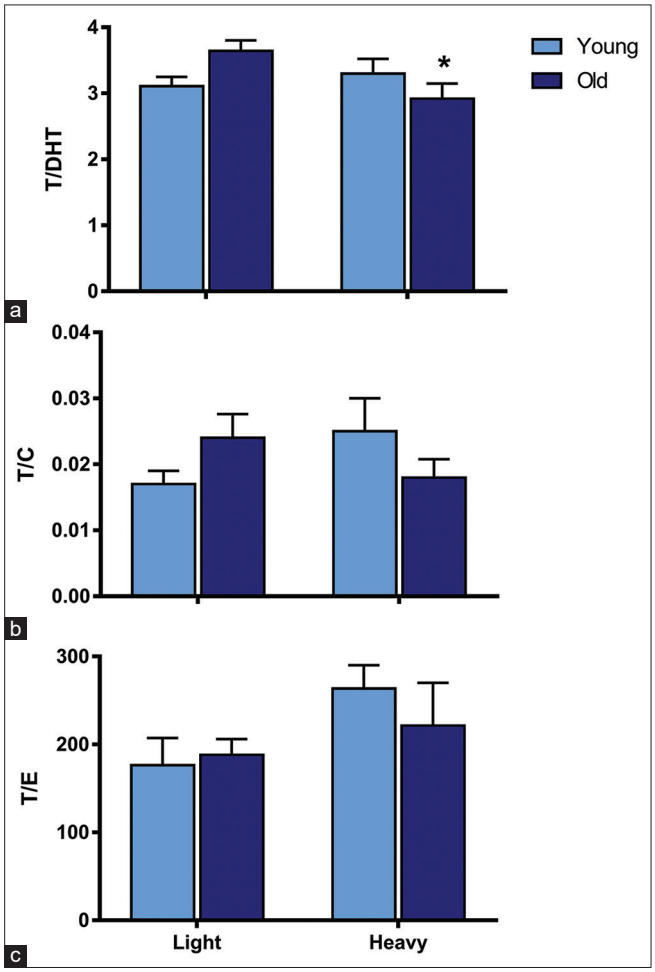

Figure 3: For both light (<50 km/week) and heavy (≥50 km/week) training, (a) T/DHT, (b) T/C and (c) T/E ratio are reported. Comparisons between young (30–55 years) and old (56–70 years) men are outlined as mean and standard error (vertical bars). Abbreviations: T/C: Testosterone/cortisol, T/E: Testosterone/estradiol, T/DHT: Testosterone/dihydrotestosterone). Significantly different: *P < 0.05, OH versus YH.

The reasons for T changes during exercise are not completely understood, although production rate, clearance, or binding capacity could be the mechanisms involved.[44] Moreover, neural systems can directly affect the HPG axis activity, as endogenous opioids are known to increase in high-intensity trained athletes.[45] Endogenous opioids (in particular β-endorphin) have an inhibitory action on the release of gonadotropin-releasing hormone, with follicle-stimulating hormone and LH inhibition. This results in disruption of the menstrual cycle in females and decreased T production in males; for these central-mediated effects, Sutton and Lazarus suggested a lack of LH spike during short-term exercise.[46] Interestingly, Hackney *et al*. hypothesized that a T decrease would be caused by direct opioid-mediated inhibition of the Leydig cells in the testicles.[47] Moreover, Vasankari *et al*. suggested that modulation of the regulatory function of the HPA is responsible for T changes during intense and prolonged (>2 h) exercise.[34,48,49]

In the present study, we have shown that exercise-induced hypogonadism is present in both age groups and, although both young and old subjects show quite low TT levels, older subjects with high training habits show lower levels than those with light activity. A different trend is observed in the younger groups, with higher TT in those training at higher levels. The authors are not aware of studies trying to explain the age-induced effects in these endocrine systems. In previous studies by Galbo and colleagues, it was suggested that hormonal levels would be related to the exercise intensity;[50,51] this was recently confirmed by Alves *et al*. who showed that exercise causes stress in the organism able to affect the endocrine system.[52,53]

In particular, C was found to increase at intensities >50%–60% of the VO_2max[54,55] while no changes were observed at intensities lower than 35% of the VO_2max.[56] Peake and colleagues demonstrated an increased C level after high-intensity interval training vs work-matched continuous exercise at moderate intensities.[57] Thus, since T has to be considered an anabolic agent and C a catabolic agent, their measure can be used to monitor and evaluate the body's response to chronic exercise-induced stress.[58] In runners and other high-volume athletes, the catabolic state seems to prevail. In endurance training, the T/C ratio is related to exercise duration.[37] Hence, a low T/C ratio results in energy production

through amino acids in the gluconeogenesis pathway with negative effects on muscle mass.[59]

In rats, the increase of urea excretion when blood T levels decrease appears to protect muscle from protein degradation.[60] Thus, it has to be considered that in runners the maintenance of a correct level of T and other anabolic hormones is essential to preserve muscle mass and repair damage to skeletal muscles.[61]

Conclusion

Training can affect andrological health and T levels in runners. However, while high training volume is associated with higher T levels in young runners, in older ones the T levels are often lower in those with higher activity. Thus, the present results suggest that gonadal hormone levels should also be properly monitored in male athletes to help them maintain appropriate exercise levels and avoid exercise-induced detrimental effects.

Ethics approval and consent to participate

The study was approved by the Ethics Committee of the Department of Biomedical Sciences of the University of Padova (HEC-DSB 0/15). Written informed consent for publication was obtained from the participants involved in the study.

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Conflicts of interest

There are no conflicts of interest.

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