Serum androgen levels and their relation to performance in track and field: mass spectrometry results from 2127 observations in male and female elite athletes

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ABSTRACT

Objective To describe and characterise serum androgen levels and to study their possible influence on athletic performance in male and female elite athletes.

Methods 2127 observations of competition best performances and mass spectrometry-measured serum androgen concentrations, obtained during the 2011 and 2013 International Association of Athletics Federations World Championships, were analysed in male and female elite track and field athletes. To test the influence of serum androgen levels on performance, male and female athletes were classified in tertiles according to their free testosterone (fT) concentration and the best competition results achieved in the highest and lowest fT tertiles were then compared.

Results The type of athletic event did not influence fT concentration among elite women, whereas male sprinters showed higher values for fT than male athletes in other events. Men involved in all throwing events showed significantly ($p<0.05$) lower testosterone and sex hormone binding globulin than men in other events. When compared with the lowest female fT tertile, women with the highest fT tertile performed significantly ($p<0.05$) better in 400 m, 400 m hurdles, 800 m, hammer throw, and pole vault with margins of 2.73%, 2.78%, 1.78%, 4.53%, and 2.94%, respectively. Such a pattern was not found in any of the male athletic events.

Conclusion Female athletes with high fT levels have a significant competitive advantage over those with low fT in 400 m, 400 m hurdles, 800 m, hammer throw, and pole vault.

INTRODUCTION

Testosterone and its chemical derivatives, androgens, have been abused by athletes since the 1950s. These molecules produce improved performances in both male and female athletes, sometimes in a systematic way, as reported in the recently disclosed documentation from experiments performed by sports scientists in the former German Democratic Republic.[1] These scientists concluded after the 1972 Olympic Games in Munich that "the effects of the treatment with androgenic hormones were so spectacular, particular in female athletes in strength dependent events, that few competitors not using the drugs had a chance of winning".

Although androgens have been widely abused by female athletes during the last few decades, obvious ethical and disciplinary limitations explain why mechanisms underlying the performance-enhancing effects of these androgens, as well as the magnitude of their effects, have not been properly addressed. However, the high incidence of such androgens in adverse analytical findings from analysis of athletes' samples suggests that the athletes at least perceive they have a material impact on athletic performance. For instance, among the 296 elite athletes serving a doping ban under the rules of the International Association of Athletics Federations (IAAF) as of 19 December 2016, 116 are females, of which 64 tested positive for androgens.[2] These findings confirm that these doping substances are the most prevalent ones among female athletes, in spite of continually improving analytical techniques and strategies to detect their abuse.[3] Additionally, the highly increased endogenous productions of androgens demonstrated by some female athletes, as well as their virilised phenotype, have been highlighted in sports and represent a subject of controversy among the scientific community.[4–9]

To address this sensitive issue, the IAAF and the International Olympic Committee respectively published regulations and recommendations governing the eligibility of women with hyperandrogenism to compete in the female category of competitions.[10 11] An Indian athlete, Dutee Chand, challenged the IAAF regulations before the Court of Arbitration for Sports (CAS).[12] The CAS panel accepted that "possessing high levels of testosterone, and thereby increased LBM (Lean Body Mass), … creates a competitive advantage", and also that there was "evidence and opinion to support the conclusion that endogenous and exogenous testosterone have identical physiological effects"; however, the panel ruled that, in order to justify the discriminatory effect the IAAF regulations have on androgen-sensitive hyperandrogenic athletes (requiring them to have treatment to lower their endogenous testosterone levels in order to continue to compete), the IAAF must also produce "sufficient scientific evidence about the quantitative relationship between enhanced testosterone levels and improved athletic performance in hyperandrogenic athletes", such as evidence of a correlation between testosterone levels and relative rankings in competitive athletics events. It suspended the IAAF regulations pending receipt of such further evidence. The purpose of this article is therefore to explore the possible relationship between serum androgen concentration (particularly serum testosterone concentration) and athletic performance.

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METHODS

Our aim was to describe and characterise serum androgen levels in athletes taking part in the 2011 (Daegu, South Korea) and 2013 (Moscow, Russia) IAAF World Championships. As a second step, we studied the influence of serum androgen levels and athletic performance in both male and female populations. All logistical, methodological (including sampling, pre-analytical conditions and analytical methods), and ethical aspects of this project have been extensively described and published elsewhere.[13–15] The project comprised a study of elite female athletes taking part in the Daegu and the Moscow IAAF World Championships, and elite male athletes taking part in the Moscow IAAF World Championships. The data obtained from male athletes competing in Daegu were not selected for the purpose of this study since the serum androgen levels were not measured by mass spectrometry, but by immunological methods.

Subjects

The subjects were athletes competing at the highest level in the different track and field events (of which there are 21 for females and 22 for males). Athletes with missing blood data were excluded from the study, as were athletes who did not start, did not finish, were disqualified, or had no results. Athletes taking part in relay races (but not taking part in individual races) were also excluded. In the female athlete group, 17.3% of athletes took part in both the 2011 and 2013 World Championships, and all their results were included in our statistical analysis. As a result, the present study relies on 1332 observations of elite female athletes and 795 observations of elite male athletes—a total of 2127 observations. A blood sample was taken from each of these athletes.

Measures

Athletes were required to go to the doping-control station at any time during their stay, provided it was at least 24 hours after their arrival in Daegu or Moscow and at least 2 hours after intense exercise. All pre-analytical conditions and analytical methods have been extensively described in previous publications.[13 14] In female athletes, samples were collected regardless their menstrual status and phase. Whole blood samples and sera were collected after 10 min of rest, in a non-fasting state, and sera were frozen at −20°C until assay. Haemoglobin (Hb) concentration was measured as part of the athlete haematological passport, as previously described.[14] All analyses for endocrine parameters were conducted in the Lausanne World Anti-Doping Agency (WADA)-accredited laboratory. Serum sex hormone binding globulin (SHBG) and luteinising hormone (LH) concentrations were determined with an Immulite 2000 (Siemens Healthcare Diagnostics SA, Zürich, Switzerland), whereas serum dehydroepiandrosterone sulfate (DHEAS) was determined with an Immulite 2000 XPi (Siemens Healthcare Diagnostics SA, Zürich, Switzerland). Measurement kits, reagents, equipments, adjustors and protocols were provided by the manufacturer. All samples, adjustors and quality controls (QC) were run with the same batch lot numbers. Finally, serum testosterone (T) and androstenedione (A4) were measured by LC-MS high resolution (Q-Exactive, ThermoFisher Scientific, Reinach, Switzerland). Free T (fT) was calculated using the Sodergard formula, with a standard average albumin concentration of 4.3 g/dL.[16] For purpose of comparison with previously published data, albumin concentration was considered at 4.3 g/dL (and not 4.0 g/dL as recommended by some authors) for fT calculation in females. For each athlete, the best performance (heats or finals) achieved during the corresponding World Championships was considered for statistical analysis.

Statistical analyses

Data distributions were assessed for normality using visual inspection, calculation of skewness and kurtosis, and the Kolmogorov-Smirnov test. In order to test for the possible effects of the type of athletic event on hormonal parameters, all athletes were assigned to one of the seven following groups: throwing events (discus throw, javelin throw, hammer throw, and shot put), jumping events (high jump, long jump, triple jump, pole vault), sprinting events (100 m, 110 m hurdles, 200 m, 400 m, 400 m hurdles), combined events (heptathlon for females and decathlon for males), middle distance running (800 m, 1500 m, and 3000 m steeple chase), long distance running (5000 m, 10 000 m, and marathon), and race walking (20 km race walking in females and 20 km and 50 km race walking in males). The effects of the type of athletic event were tested with a one-way analysis of variance (ANOVA) on log-transformed age and endocrine parameters across the considered groups and Tukey HSD (Spjotvoll/Stoline) post hoc test when appropriate. In order to test the influence of serum androgen levels on athletic performance, in each of the 21 female athletic events and 22 male athletic events, athletes were classified in tertiles according to their fT concentration. Then, the athletic performances and Hb concentrations of the highest and lowest fT tertiles were compared by using non-paired Student's t-test. These different athletic events were considered as distinct independent analyses and adjustment for multiple comparisons was not required. Classification in tertiles according to the T (both genders) and Hb (female gender) concentrations were also performed and appear online (see supplementary tables 6-13). When appropriate, a χ^2 test was used. Correlations were tested by the Pearson correlation test. A value of $p<0.05$ was considered statistically significant. All data analyses were performed using Statistica version 7.1 (StatSoft, France).

RESULTS

For the female group of athletes, their ages and concentrations of serum T, A4, DHEAS, LH and SHBG, as well as the calculated fT, are presented in table 1. Among the 1332 female observations, 44 showed an fT concentration >29.4 pmol/L.[17] Twenty-four female athletes showed a T concentration >3.08 nmol/L which has been calculated to represent the 99th percentile in a previous normative study in elite female athletes.[13] Among these 24 individuals, nine were diagnosed with a condition of hyperandrogenic disorder of sex development (DSD), nine were later found to have been doping, and six athletes were impossible to classify. This also explains the high calculated standard deviation for T and fT in some groups of athletic events (table 1). Long distance runners showed lower A4 concentrations than sprinter and middle distance runners, and lower DHEAS concentrations than sprinters, race walkers and throwers.

For the male group of athletes, their ages and serum T, A4, DHEAS, LH and SHBG concentrations, and the calculated fT, are presented in table 2. Among the 795 male athletes, 101 showed an fT value <0.23 nmol/L. Fourteen of them were sprinters, 14 were middle distance runners, 21 were long distance runners, 16 were race walkers, 20 were jumpers, 13 were throwers, and two were combined events specialists. The male sprinters showed a higher fT concentration than the other male athletes. Interestingly, throwers showed significantly lower T and SHBG concentrations than the other male athletes.

Table 1 Age and androgenic parameters in the female population

	n	Age (years)	fT (pmol/L)	T (nmol/L)	A4 (nmol/L)	DHEAS (µmol/L)	LH (IU/L)	SHBG (nmol/L)
Sprinting	390	25 (22–27)	9.5 (6.0–13.0)	0.73 (0.52–0.99)	3.38 (2.50–4.34)*	6.18 (4.13–9.40)*	3.35 (1.75–5.86)	56.5 (40.7–79.4)
Middle distance	186	25 (23–28)	8.1 (5.0–12.0)	0.64 (0.46–0.92)	3.26 (2.39–4.50)*	5.99 (3.72–8.86)	3.72 (1.78–6.74)	56.5 (42.8–75.3)
Long distance	165	28 (24–31)	7.2 (4.8–9.6)	0.55 (0.43–0.78)	2.80 (2.10–3.80)	4.61 (2.77–7.15)	2.86 (1.60–5.09)	55.8 (41.2–73.7)
Walking	97	25 (23–29)	7.5 (5.0–11.0)	0.58 (0.44–0.82)	3.20 (2.27–4.21)	7.06 (4.10–10.80)**	3.05 (1.36–4.38)	52.5 (35.1–70.9)
Jumping	220	27 (23.5–29)	7.9 (5.0–11.0)	0.68 (0.48–0.92)	2.32 (2.47–4.60)	5.69 (3.79–8.46)	3.78 (2.11–6.52)	60.0 (44.10–78.9)
Throwing	211	27 (23–29)	10.5 (7.1–15.1)	0.72 (0.56–0.98)	3.24 (2.32–5.40)	6.61 (4.34–9.37)**	3.38 (2.07–5.24)	44.2 (29.0–66.8)
Combined events	53	26 (23–28)	6.5 (4.8–9.5)	0.62 (0.42–0.79)	3.00 (2.01–3.42)	5.51 (3.75–8.86)	3.67 (1.84–5.81)	61.6 (46.7–87.7)
All	1332	26 (23–29)	8.5 (5.7–12.3)	0.67 (0.48–0.90)	3.22 (2.34–4.33)	5.92 (3.82–9.05)	3.41 (1.80–5.77)	55.3 (38.9–74.0)

Data are presented as median (25th percentile–75th percentile].
Different from Long distance: *p<0.05, **p<0.01.
A4, androstenedione; DHEAS, dehydroepiandrosterone sulfate; fT, free testosterone; LH, luteinising hormone; SHBG, sex hormone binding globulin; T, testosterone.

The comparison of the highest and lowest female fT tertiles and their associated athletic performances in running events is presented in table 3. When compared with the lowest fT tertile, the highest fT tertile demonstrated significantly better performances in 400 m, 400 m hurdles, and 800 m with calculated differences of 2.73%, 2.78%, and 1.78%, respectively.

In other non-running events (table 4), hammer throwers and pole vaulters with high fT concentrations performed better (+4.53% and 2.94%, respectively) than their peers with low fT concentrations.

In male elite athletes, no significant difference in performance was noted when comparing the lowest and the highest fT tertiles.

DISCUSSION

To the best of our knowledge, this study is the first to report serum androgen concentrations in such a large number of elite male and female athletes. In the female athlete group, the statistical analysis on performance and androgen levels, conducted using only the 2013 Moscow data, confirmed the statistical findings obtained from the 2011 Daegu dataset. This is why both female datasets (from 2011 and 2013) were merged and as a consequence some duplicate observations at the 2-year interval were included. This oversampling bias is negligible, since androgen level outliers from the 2011 Daegu dataset did not appear in the 2013 Moscow dataset as a consequence of either IAAF antidoping or hyperandrogenism regulations enforcement.[10]

Our study design cannot provide evidence for causality between androgen levels and athletic performance, but can indicate associations between androgen concentrations and athletic performance. Thus, we deliberately decided not to exclude performances achieved by females with biological hyperandrogenism and males with biological hypoandrogenism whatever the cause of their condition (oral contraceptives, polycystic ovaries syndrome, disorder of sex development, doping, overtraining). As a consequence, the calculated mean fT value in the present study is higher than the 8.06 pmol/L median value previously reported in a similar female population.[13] Oral contraceptive intake had not been registered during the 2013

Table 2 Age and androgenic parameters in the male population

	n	Age (years)	fT (nmol/L)	T (nmol/L)	A4 (nmol/L)	DHEAS (µmol/L)	LH (IU/L)	SHBG (nmol/L)
Sprinting	229	25 (22–27)	0.39 (0.31–0.48)	17.6 (13.8–22.0) ††	2.02 (1.64–2.60)	8.28 (5.99–10.88)	2.94 (2.06–4.04)	31.2 (24.9–38.0) ††
Middle distance	117	24 (22–28)	0.36 (0.28–0.42) *	15.91 (13.0–21.0) ††	2.15 (1.74–2.90)	8.48 (6.26–10.91) ‡‡	2.64 (2.06–3.62)	32.6 (26.4–41.7) ††
Long distance	102	27 (23–30)	0.31 (0.25–0.38) **	15.4 (11.6–19.0) †	1.91 (1.55–2.40)	6.20 (4.55–10.03)	2.74 (2.04–3.54)	34.5 (26.8–42.4) ††
Walking	94	26.5 (25–30)	0.34 (0.26–0.40) **	15.0 (11.8–18.2) †	2.14 (1.59–2.69)	7.57 (4.92–10.25)	2.77 (2.16–4.06)	28.6 (24.5–37.0) ††
Jumping	113	26 (23–29)	0.34 (0.26–0.42) **	15.7 (12.0–19.2) ††	2.13 (1.69–2.67)	8.86 (6.17–11.83) ‡	2.74 (1.96–3.91)	32.2 (26.6–37.5) ††
Throwing	115	28 (24–31)	0.30 (0.26–0.36) **	12.4 (9.8–15.4)	2.07 (1.59–2.88)	8.72 (6.05–13.66) ‡‡	3.45 (2.41–5.01)	21.6 (17.0–27.0)
Combined events	25	25 (23–27)	0.37 (0.31–0.42)	16.1 (13.7–21.5)	2.28 (1.87–2.67)	9.58 (6.76–11.12)	3.06 (2.26–4.41)	31.5 (24.7–41.9) ††
All	795	25 (23–29)	0.34 (0.27–0.43)	15.6 (12.1–19.8)	2.06 (1.65–2.65)	8.20 (5.72–11.99)	2.94 (2.11–4.10)	30.6 (23.5–37.9)

Data are presented as median (25th percentile–75th percentile).
Different from Sprinting: *p<0.05, **p<0.01. Different from Throwing: †p<0.05, ††p<0.01. Different from Long distance: ‡p<0.05, ‡‡p<0.01.
A4, androstenedione; DHEAS, dehydroepiandrosterone sulfate; fT, free testosterone; LH, luteinising hormone; SHBG, sex hormone binding globulin; T, testosterone.

Table 3 Comparison of the lowest and highest fT tertiles and their associated athletic performances in female running events

Event	n	All athletes	Lowest fT tertile	Highest fT tertile
100 m				
Time s	112	11.88 (0.88)	11.78 (0.83)	12.09 (0.97)
fT pmol/L		(1.4–32.8)	(1.4–8.2)	(12.1–32.8)
T nmol/L		0.90 (0.52)	0.53 (0.18)	1.32 (0.63)
100 m H				
Time s	73	13.15 (0.48)	13.02 (0.46)	13.24 (0.54)
fT pmol/L		(1.0–29.6)	(1.0–6.6)	(9.9–29.6)
T nmol/L		0.75 (0.33)	0.52 (0.20)	0.92 (0.34)
200 m				
Time s	71	23.43 (0.90)	23.28 (0.74)	23.65 (1.11)
fT pmol/L		(1.0–28.2)	(1.0–6.3)	(11.1–28.2)
T nmol/L		0.78 (0.48)	0.47 (0.15)	1.11 (0.62)
400 m				
Time s	67	52.23 (2.56)	52.60 (3.30)	51.16 (1.06)*
fT pmol/L		(1.2–124.4)	(1.2–6.5)	(13.0–124.4)
T nmol/L		2.82 (7.41)	0.45 (0.21)	7.08 (11.64)
400 m H				
Time s	67	56.34 (2.65)	57.38 (3.53)	55.78 (1.60)*
fT pmol/L		(1.4–174.5)	(1.4–7.9)	(12.4–174.5)
T nmol/L		1.03 (1.13)	0.54 (0.26)	1.68 (1.63)
800 m				
Time s	64	121.80 (5.42)	122.68 (3.71)	120.50 (2.90)*
fT pmol/L		(1.1–469.3)	(1.1–7.0)	(12.2–469.3)
T nmol/L		1.47 (4.03)	0.40 (0.14)	3.26 (6.60)
1500 m				
Time s	66	250.16 (6.42)	250.00 (3.23)	250.65 (7.10)
fT pmol/L		(0.6–48.7)	(0.6–7.0)	(10.8–48.7)
T nmol/L		0.79 (0.49)	0.50 (0.27)	1.12 (0.62)
3000 m SC				
Time s	56	581.61 (17.39)	579.81 (17.74)	581.03 (18.70)
fT pmol/L		(2.0–43.2)	(2.0–4.9)	(8.0–43.2)
T nmol/L		0.73 (0.54)	0.39 (0.15)	1.20 (0.66)
5000 m				
Time s	40	932.67 (39.73)	932.80 (32.4)	935.80 (48.30)
fT pmol/L		(2.8–51.8)	(2.8–6.1)	(8.0–51.8)
T nmol/L		0.73 (0.59)	0.41 (0.14)	1.07 (0.84)
10 000 m				
Time s	33	1912.6 (55.6)	1903.6 (61.8)	1913.8 (50.6)
fT pmol/L		(2.7–26.4)	(2.7–4.5)	(9.0–26.4)
T nmol/L		0.59 (0.27)	0.33 (0.13)	0.85 (0.21)
Marathon				
Time s	92	9726.6 (790.9)	9921.3 (1018.9)	9620.1 (736.5)
fT pmol/L		(2.1–363.6)	(2.1–5.6)	(9.0–363.6)
T nmol/L		0.97 (2.55)	0.41 (0.14)	1.85 (4.23)

Data are presented as mean (SD) or (min–max).
Different from the lowest fT tertile: *p<0.05.
fT, free testosterone; H, hurdles; SC, Steeple Chase; T, testosterone.

Table 4 Comparison of the lowest and highest fT tertiles and their associated athletic performances in female non-running events

Event	n	All athletes	Lowest fT tertile	Highest fT tertile
Discus				
Distance m	48	60.18 (4.24)	59.58 (4.97)	60.69 (4.34)
fT pmol/L		(2.1–33.4)	(2.1–7.5)	(12.7–33.4)
T nmol/L		0.82 (0.44)	0.60 (0.24)	1.16 (0.53)
Hammer throw				
Distance m	54	69.31 (4.34)	67.76 (2.75)	70.83 (5.16)*
fT pmol/L		(1.0–50.4)	(1.0–8.5)	(13.1–50.4)
T nmol/L		0.82 (0.40)	0.62 (0.31)	1.13 (0.36)
Shot put				
Distance m	54	18.21 (1.33)	17.94 (1.58)	18.54 (1.23)
fT pmol/L		(1.8–319.9)	(1.8–10.0)	(16.8–319.9)
T nmol/L		1.03 (1.57)	0.57 (0.22)	1.72 (2.45)
Javelin				
Distance m	55	60.40 (4.35)	61.9 (4.64)	60.37 (4.40)
fT pmol/L		(2.2–26.8)	(2.2–7.3)	(9.9–26.8)
T nmol/L		0.73 (0.27)	0.59 (0.21)	0.90 (0.16)
Long jump				
Distance m	62	6.46 (0.28)	6.39 (0.34)	6.47 (0.30)
fT pmol/L		(2.1–24.2)	(2.1–6.9)	(10.4–24.2)
T nmol/L		0.80 (0.43)	0.53 (0.23)	1.00 (0.26)
Triple jump				
Distance m	54	14.00 (0.49)	14.05 (0.52)	13.95 (0.43)
fT pmol/L		(1.4–242.8)	(1.4–6.4)	(9.2–242.8)
T nmol/L		0.92 (1.59)	0.42 (0.16)	1.66 (2.54)
High jump				
Distance m	56	1.91 (0.07)	1.89 (0.06)	1.90 (0.06)
fT pmol/L		(3.6–23.4)	(3.6–6.0)	(8.9–23.4)
T nmol/L		0.74 (0.42)	0.48 (0.21)	1.07 (0.51)
Pole vault				
Distance m	48	4.51 (0.18)	4.41 (0.18)	4.54 (0.17)*
fT pmol/L		(2.0–22.9)	(2.0–6.3)	(8.7–22.9)
T nmol/L		0.78 (0.31)	0.63 (0.28)	0.98 (0.31)
20 km RW				
Time s	97	5600 (617)	5680 (235)	5647 (232)
fT pmol/L		(1.8–31.9)	(1.8–5.9)	(9.7–31.9)
T nmol/L		0.62 (0.29)	0.43 (0.16)	0.87 (0.30)
Heptathlon				
Point	53	6121 (309)	6095 (353)	6096 (263)
fT pmol/L		(1.8–30.4)	(1.8–5.7)	(8.9–30.4)
T nmol/L		0.69 (0.36)	0.47 (0.12)	1.02 (0.43)

Data are presented as mean (SD) or (min–max).
Different from the lowest fT tertile: *p<0.05.
fT, free testosterone; RW, race walking; T, testosterone.

World Championships, but these medicines were reported to be used by approximately 15% of elite female athletes.[13]

Key findings

As oral contraceptives increase SHBG concentration and T bioavailability, we performed the main statistical analysis on fT. Given criticism of the inaccuracy of the Sodergard formula, we calculated fT by using the Sartorius formula and confirmed our statistical findings.[18 19] We also confirmed that the type of athletic event does not influence T and fT concentrations in elite females.[13] Moreover, we found that female endurance runners showed decreased A4 and DHEAS concentrations when compared with other athletes. This finding can be explained by the suppressive effect of endurance training on adrenocorticotropic hormone and the adrenal production of T.[20] As far as male athletes are concerned, sprinters showed higher values for fT, but not for T, than other athletes.

No result including fT has been published on this matter so far; the only available source is the article by Cardinale and Stone who also reported, on a small number of subjects, higher

T concentrations in male sprinters when compared with handball and soccer players.[21] The observed low T concentration in male throwers is an unexpected result. This trend is observed in all throwing events: mean T concentrations were 14.1 nmol/L, 12.6 nmol/L, 11.2 nmol/L, and 14.5 nmol/L in discus, hammer throw, shot put, and javelin, respectively. All these results are below the T concentration measured in male race walkers and marathon runners which are athletic events where hypoandrogenism is a commonly reported condition.[22] Male throwers not only showed low T but also low SHBG concentrations. These differences are not explained by age or ethnic background in our subgroup of male throwers.

One explanation could be the higher prevalence of doping with exogenous androgens in this subgroup. Indeed, it has been reported that oral administration of androgens decreases both T (a well-known withdrawal phenomenon experienced when the athletes are approaching competitions and associated urinary anti-doping tests) and SHBG concentrations.[23 24] Recently, Rasmussen *et al* showed that a significant proportion of former androgen abusers exhibit moderately or notably lowered testosterone levels years after cessation of androgen abuse.[25] However, our male throwers did not show decreased LH concentrations (a reported consequence of doping with androgens via the negative feedback loop of the hypothalamic-pituitary-gonadal axis).[26] Although it has not been measured in the present study, throwers are also likely to be athletes with the highest body mass index and fat mass. Hence, the known negative influence of fat mass on SHBG concentration and T bioavailability may possibly account for the low T and SHBG concentrations reported in male throwers in our study.[27]

In female athletes, a high fT concentration appears to confer a 1.8–2.8% competitive advantage in long sprint and 800 m races. Taking into account a linear dose–response relationship between serum androgen levels and athletic capacity, it is possible that the magnitude of this advantage will be even greater for an androgen-sensitive female athlete with T or fT concentrations within the normal male range.[28] A possible explanation for these findings is the important contribution of oxidative metabolism in the total energy spent to run a 400 or 800 m race. Duffield *et al* calculated that in females the aerobic/anaerobic energy system contribution is 45%/55% for 400 m and 70%/30% for 800 m.[29] As androgens are erythropoietic hormones, it is tempting to hypothesise that female athletes with high T and fT levels show high Hb concentrations which in turn increase the oxygen-carrying capacity and (non-bicarbonate) extracellular buffering capacity[30]—both of which are crucial when running 400 m, 400 m hurdles or 800 m races. For each of these three running events, fT concentration significantly ($p<0.05$) positively correlated with Hb concentration, and within these groups, athletes with the highest fT levels showed higher Hb concentrations than athletes with the lowest fT levels (table 5). This average difference in Hb concentration is approximately 0.6 g/100 mL. However, in these three events, we found no significant correlation between Hb concentration and performance (table 5), and when athletes were clustered in tertiles according to their Hb concentrations, no difference was noted in performances between the high and low Hb (see online supplementary results).

Taken together, these results show that whereas fT positively influences Hb, fT concentration is a stronger determinant of performance in the 400 m, 400 m hurdles and 800 m than Hb concentration. Increased lean body mass, mental drive and aggressiveness, which are also known to be influenced by androgens, provide alternative explanations, but these parameters have not been measured in the present study.[31]

Table 5 Comparison of the haemoglobin concentrations in the lowest and highest fT tertiles and correlation between haemoglobin concentration and free testosterone or athletic performance in female 400 m, 400 m hurdles and 800 m

400 m		Hb
	Lowest fT tertile	13.41 (0.90)
	Highest fT tertile	14.03 (1.03) *
	Correlation fT vs Hb	r=0.26 †
	Correlation performance vs Hb	r=−0.12
400 m H		Hb
	Lowest fT tertile	13.25 (0.88)
	Highest fT tertile	13.88 (0.99) *
	Correlation fT vs Hb	r=0.29 †
	Correlation performance vs Hb	r=0.04
800 m		Hb
	Lowest fT tertile	13.47 (0.78)
	Highest fT tertile	14.16 (1.09) *
	Correlation fT vs Hb	r=0.26 †
	Correlation performance vs Hb	r=0.03

Data are presented as mean (SD).
Different from the lowest tertile *p<0.05. Significant correlation †p<0.05.
fT, free testosterone; H, hurdles; Hb, haemoglobin concentration in g/100 mL.

Free testosterone concentration and throwing events

The relationship between high fT concentration and better performances by female athletes in hammer throw and pole vault (+4.5% and +2.9%, respectively) is a finding reported for the first time. In order to perform at elite level in these two events, athletes must achieve a high level of power and strength, supported by an increased lean body mass. Although an effect of high androgen levels on these functional and anthropometric characteristics is likely, performance in other strength and power events like shot put, javelin or long jump does not seem to be influenced by the fT concentration in our study. Pole vault and hammer throw are the athletic events which require the highest spatial abilities. For instance, hammer throw requires three final high speed turns (more than 720°/s), inside a 7-foot diameter ring, to release a 4 kg hammer at a terminal speed of 27 m/s with an optimal release angle between 43° and 44° to the horizontal plan and within a cage sector of only 34.9°. There are well known sex differences in spatial abilities as measured with the mental rotation task (MRT), where males have an advantage over females.[32] This difference is of critical importance, since the performance at the MRT is associated with the type of sports practised and the level of expertise. In a recent study, including non-athletes, orienteers, gymnasts and endurance runners, Schmidt *et al* showed that athletes outperformed non-athletes at the MRT. Interestingly, athletes with high mental rotation demand, like gymnasts (egocentric transformation) and orienteers (allocentric transformation), showed the best results at the MRT.[33] By using functional MRI assessment, two research groups showed a female-like activation pattern in mental rotation-related brain areas in individuals with complete androgen insensitivity syndrome, indicating that the sexual differentiation of visuospatial neural activation is not directly influenced by sex chromosomal composition, but is determined by exposure to androgens.[34 35]

Speculation as to mechanisms underpinning our findings

Our hypothesis is that, in addition to their recognised effect on aggressiveness and risk-taking behaviours, androgens exert their ergogenic effects on some sportswomen through better visuospatial neural activation. This assumption, which may be of critical importance in acrobatic, team or racket sports, warrants

further research. Unlike female athletes, males with the highest fT concentration did not outperform those with the lower fT concentration in any of the events. Our results obtained in both sexes could confirm the recent hypothesis from Bird *et al*, suggesting that in terms of gains in muscle mass and strength, females have the capacity to gain a greater relative increase from androgen use than males.[36] Hence, when the results from male and female athletes are pooled, the relationship linking T concentration to athletic performance would look more like a sigmoid curve, with the steepest portion found between above the female range upper limit and below the male lower limit.

In conclusion, our original work confirmed the weak influence of particular athletic events on circulating androgens levels in females, whereas male throwers showed low T and SHBG concentrations but normal fT levels. Such a finding might be a consequence of either a higher prevalence of doping with androgens or a higher adiposity in this group of athletic events. In female 400 m, 400 m hurdles, 800 m, hammer throw and pole vault, high fT concentration is associated with a higher (from 1.8% to 4.5%) level of athletic performance when compared with competitors with low fT. In addition to the well-known performance-enhancing effects of androgens on lean body mass, erythropoiesis, mental drive and aggressiveness, the results obtained in pole vaulters and hammer throwers seem to confirm that females with high levels of androgens may also benefit from a competitive advantage through improved visuospatial abilities.

What are the findings?

- In females, the serum testosterone level is not influenced by the type of athletic events, whereas androstenedione and DHEAS are decreased in endurance runners.
- Male throwers have lower testosterone and SHBG concentrations than other elite male athletes.
- In 400 m, 400 m hurdles, 800 m, hammer throw and pole vault, female athletes with high testosterone levels benefit from a 1.8% to 4.5% competitive advantage over other female competitors with normal androgen levels.

How might it impact on clinical practice in the future?

- The quantitative relationship between enhanced testosterone levels and improved athletic performance should be taken into account when the eligibility of women with hyperandrogenism to compete in the female category of competition is discussed.

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Contributors SB was involved in the study design, statistical analysis and manuscript drafting. PYG was involved in the study design, data collection, and manuscript drafting.

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