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Androgen receptor CAG repeats and body composition among Ariaal men

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Summary

To determine the population variation in the androgen receptor (AR) and its association with body composition in a subsistence population, we sampled 87 settled and 65 nomadic males ages 20+ among the Ariaal of northern Kenya. Anthropometric measures included height, body mass index, fat-free mass (FFM), upper arm muscle plus bone area (AMPBA), % body fat (%BF), suprailliac skinfold (SISF), and waist-to-hip ratio. Salivary testosterone (T) was determined from both morning (Am T) and afternoon (Pm T) samples. Hair roots were obtained for genotyping AR CAG repeat length. AR CAG repeat length did not vary between the two sub-groups (overall value = 22.6 ± 3.1). Multiple regression models, controlling for age and residence, indicate that Pm T was positively associated with all measures of body composition. AR CAG repeat length was a significant positive predictor of height, FFM, %BF, SISF and waist circumference. There was a significant negative Pm T by AR CAG repeat length interaction in predicting all anthropometric measures but AMPBA. These findings provide evidence for population variation in AR CAG repeat length and suggest that both T and AR CAG length play a role in body composition in this extremely lean population.

Introduction

Testosterone levels vary across populations, with subsistence populations showing lower levels relative to industrialized populations (Ellison *et al.*, 2002). Lower testosterone levels among men in subsistence populations are thought to reflect energetic limitations (Ellison & Panter-Brick, 1996; Campbell *et al.*, 2006a; Ellison, 2001). Bribiescas (2001, 2005) and Bribiescas & Hickey (2006) have suggested that lower testosterone levels under conditions of poor nutrition would allow the allocation of energy away from muscle toward other somatic functions, including the immune system (Muehlenbein & Bribiescas, 2005).

Recent findings suggest a relationship between testosterone levels and chronic undernutrition in subsistence populations. Testosterone has been positively associated with markers of energy status including weight, biceps skinfold and midarm circumference among the Tamang of Nepal (Ellison & Panter-Brick, 1996), body fat among the Turkana and Ariaal of Kenya (Campbell *et al.*, 2003, 2006a,b) and fat-free mass (FFM) among men in Harare, Zimbabwe (Lukas *et al.*, 2005). Furthermore, Lukas *et al.* (2004) found a relationship between height and afternoon testosterone values in men under 60, which they interpret as an indication that the effects of testosterone may be primarily associated with the development of overall body size (and potential muscle mass) at puberty, rather than the maintenance of muscle during adulthood per se.

Previous analyses, however, have not taken into account the potential effects of the androgen receptor (AR). As the number of CAG repeats in the AR increases, the efficiency with which the AR receptor transduces the cellular effects of testosterone is reduced (Beilin *et al.*, 2000), modulating the effect of testosterone on androgenic tissue, including spermatogenesis and bone mass (Zitzmann & Nieschlag, 2003). The number of AR CAG repeats has been associated with age-related changes in

testosterone (Krithivas *et al.*, 1999; Walsh *et al.*, 2005). In addition, the number of CAG repeats has been positively associated with body mass index (BMI) (Alevizaki *et al.*, 2003), body fat (Zitzmann *et al.*, 2003) and FFM (Walsh *et al.*, 2005), but not the effects of testosterone on muscle mass (Woodhouse *et al.*, 2003).

Thus, we chose to investigate the potential role of AR CAG repeat length on body composition among the Ariaal, pastoralists of northern Kenya. Studies demonstrating shorter CAG repeats among both Africans (Kittles *et al.*, 2001; Esteban *et al.*, 2006) and African-Americans (Kittles *et al.*, 2001) suggest that the Ariaal may also exhibit shorter CAG repeats, increasing the impact of testosterone on body composition in this population. Previous research has demonstrated both chronic undernutrition and low testosterone levels among the Ariaal, along with a lack of age-related decline in testosterone (Campbell *et al.*, 2003, 2006b), accentuating the role of energy limitation. In addition, the existence of settled and nomadic sub-populations that are culturally and genetically similar but vary in terms of ecology allowed for the investigation of gene by environment interactions. Thus, the Ariaal are an apt population for investigating the role of the AR in modulating the effects of testosterone on body composition.

Based on earlier results, we expected to find shorter CAG repeats on an average among the Ariaal as compared to non-African populations. Furthermore, as the AR mediates the androgenic effects of testosterone on target tissues, we predict that individuals with fewer AR CAG repeats would show a stronger effect of testosterone on body size and body composition.

Materials and methods

Study site

The Ariaal are pastoral nomads inhabiting both upland and lowland regions around the Ndoto mountains in Marsabit District, Kenya. First appearing in oral history in the 1880s, they are derived from groups of poor Rendille and Samburu who banded together to build up their herds in the mountains. Culturally, they still exhibit features of both Rendille and Samburu, including Samburu age-set rituals and Rendille annual camel blessings (Fratkin, 1998).

In terms of subsistence, the lowland Ariaal herd camels, which tolerate the arid conditions well, but are bothered by ticks at higher elevations. These nomads depend on their animals for nutrition in the form of milk, blood and meat. Based on dietary survey among women, milk is the overwhelming staple diet throughout the year (Fujita *et al.*, 2004). Similar quantitative data are not available for the men. Lowogosa, the nomadic encampment we sampled for this study is located approximately 45 min worth of travel from the settlement of Korr and 3 h by vehicle from the town of Logologo. The nearest clinic is in Ngrunit about 40 min away. Children do not attend elementary school.

In contrast, upland Ariaal herd cattle, which need more water and are not bothered by ticks. In addition, the upland Ariaal also tend crops, primarily maize. Based on dietary survey among women, maize meal, sugar and fat are noted to be the predominant food with milk a small part of the diet (Fujita *et al.*, 2004). Again, similar data are not available for the men. In Songa, the village we sampled, irrigation is used to support the production of crops including oranges which are sold in the nearby town of Marsabit, approximately 45 min away. Songa also has an elementary school and a nurse's station.

All procedures were approved by the Institutional Review Boards at Boston University. The study was explained to all participants and consent was obtained prior to data collection.

Sample

We sampled 102 settled men from Songa and 103 nomadic men from Lowogoso in August of 2005. The sample was stratified by 10-year age groups: 20–29, 30–39, 40–49, 50–59, 60+. We obtained hair samples from 156 of these men, including 87 settled men and 69 nomadic men. The other 50 men lacked sufficient hair to obtain a sample, either because of baldness or the fact that they had shaved their heads.

Measures

Anthropometrics

Anthropometric measures included height, weight, arm, waist and hip circumference and four skinfolds: triceps, subscapular, midaxillary, and periumbilical. Derived measures include % body fat (%BF), calculated from skinfolds based on the D-W equations (Durnin & Womersley, 1974). Because the D-W equations are based on a Caucasian sample, they may provide absolute values of %BF that are not directly comparable with other populations. However, they should provide a relatively consistent measure of %BF within the present study population. We also calculated arm muscle plus bone area (AMPBA), calculated as $[\text{MUAC} - (\pi\text{I} \times \text{TCSF}/10)]^2/4$ where MUAC is mid upper arm circumference and TCSF is the triceps skinfold (Gurney & Jellife, 1973). FFM was calculated as weight (kg) * (100 − %BF). Waist-to-hip ratio (WHR) was calculated as waist circumference/hip circumference. We chose to use waist circumference rather than WHR in our regression analyses because several studies have

concluded that it is a better measure of abdominal obesity (Pouliot *et al.*, 1994; Clasey *et al.*, 1999).

Age

During interviews, ages were estimated with reference to an event calendar and age set membership, and further ambiguities checked with local assistance (see Gray & Campbell, 2005 for further details).

Salivary testosterone

Saliva samples were collected using standard methods (Ellison, 1988) including stimulation of saliva with Original flavoured Carefree gum. Morning samples were collected within 15 min of 09.00 h, while afternoon saliva samples were collected within 15 min of 16.00 h. Sodium azide was added as a preservative. Samples were stored at ambient temperature for approximately 1 month, then frozen until assayed in the Reproductive Ecology Laboratory at Harvard University. Assay procedures relied on standard RIA techniques based on modifications of a commercially available kit obtained from Diagnostic Systems Laboratories (Dayton, TX, USA) (see methods in Campbell *et al.*, 2003). The inter-assay coefficient of variation was 15%. The intra-assay coefficient of variation was 7%. One hundred and fifty-three morning (Am) testosterone values obtained for the individuals were genotyped. Four of those values were 3 or more SDs from the mean and were removed. One hundred and fifty-two afternoon (Pm) testosterone values were obtained. Two values differed more than three SDs and were removed. This left a sample size of 149 and 150 for analyses involving hormonal values.

AR genotyping

Hair samples with roots were obtained by plucking, and immediately placed in zip lock bags for transportation to Mike Sorenson's lab at Boston University. Samples were stored in a −20 °C freezer until analysis. Bulbs were removed from three or four hairs under a dissecting microscope, and DNA was extracted with DNeasy kits (Qiagen, Valenica, CA, USA) with the addition of 30 μL of 100 mg/mL DTT (dithiothreitol) to the digestion buffer.

The AR CAG tri-nucleotide repeat was typed with a polymerase chain reaction (PCR) mix containing 1.25 μM forward primer (TCCAGAATCTGTTCCAGAGCGTGC) and 1.25 μM reverse primer (GCTGTGAAGGTTGCTGTTCCTCAT), 2.5 mM dNTP, 2.5 mM $MgCl_2$, 0.625 units AmpliTaq Gold (Applied Biosystems, Foster City, CA, USA), 1× Buffer (Applied Biosystems), 3 μL DNA template in a total volume of 25 μL. The reverse primer for AR was fluorescently labelled with VIC (Applied Biosystems). Cycle conditions were: 8 min denaturation at 95 °C, 40 cycles of 30 sec denaturation at 95 °C, 30 sec annealing at 55 °C, 1 min extension at 72 °C and one final extension of 7 min at 72 °C. PCR products were analysed on an ABI 3100 genetic analyzer using GeneMapper 3.7 (Applied Biosystems).

Four random samples were sequenced to confirm the identity of the AR locus and the number of CAG repeats. The number of trinucleotide repeats was calculated by subtracting 214 bp from the PCR product length then dividing by three. The number of repeats ranged from 15 to 34.

Statistical analysis

Androgen receptor CAG repeat length showed no significant main effect on body composition or age as a continuous variable, so we split AR CAG repeat length into high and low groups. We first tried a median split (<=22 vs. >22), as used previously (Walsh *et al.*, 2005), but a split at 20 (<=20 vs. >20) as used by Harkonen *et al.* (2003) produced stronger results; so we chose to use it for the remaining analyses.

Next, to determine if CAG repeat length had an impact on age related patterns of testosterone, we ran separate linear regression models with Am and Pm salivary testosterone as the dependent variable and AR CAG repeat length as the predictor. Age and residence were included as covariates. Given our cross-sectional data, we expected the impact of AR CAG repeat length, if any, to show up as an interaction between CAG repeat length and age. We modelled the interaction of CAG repeat length and testosterone as linear, as done previously (Krithivas *et al.*, 1999).

Then, to determine the relationship of AR CAG repeat length and testosterone on body composition, we ran separate regression analyses for height, BMI, FFM, AMPBA, %BF, and WHR. Age and residence were included as covariates, and Pm testosterone, AR CAG repeat length and their interaction were included as predictors. Again, the interaction of testosterone with AR CAG length was modelled as linear, based on previous findings demonstrating a significant effect (Walsh *et al.*, 2005). We checked for interactions between all of the predictive variables, and where there was a significant interaction, it was retained in the model when additional variables were added. Models using Am testosterone yielded similar results, but were highly dependent on individuals with the three highest Am testosterone values and are not shown here.

Results

Table 1 shows measures of body composition for the entire sample as well as by residence. The overall average BMI of 17.8 ± 1.9 kg/m^2 is less than the suggested cut-off of 18.5 kg/m^2 indicative of chronic energy deficiency (Ferro-Luzzi *et al.*, 1992); the overall average body fat of

Table 1 Comparison of body composition between settled and nomadic Ariaal males

Variable	Overall	Settled	Nomadic
N	156	87	69
Age (years)			
Height (cm)	172.4 ± 6.6	172.2 ± 6.7	172.6 ± 6.5
Weight (kgs)	52.9 ± 7.1	53.4 ± 7.8	52.4 ± 7.1
Body mass index (wt/ht2)	17.8 ± 1.9	18.0 ± 2.1	17.5 ± 1.6
Arm circumference (mm)	23.1 ± 2.1	23.2 ± 2.1	23.1 ± 2.1
Waist circumference (mm)	71.0 ± 5.9	71.8 ± 6.8	70.1 ± 4.5***
Hip circumference (mm)	86.4 ± 5.2	87.6 ± 5.3	84.9 ± 4.6+
Waist hip ratio (WHR)	0.82 ± 0.05	0.82 ± 0.05	0.83 ± 0.04
Subscapular skinfold (mm)	7.5 ± 2.5	7.7 ± 3.0	7.4 ± 1.6
Midaxillary skinfold (mm)	5.3 ± 1.7	5.5 ± 2.1	5.1 ± 0.8
Triceps (mm)	4.9 ± 1.8	4.9 ± 2.0	4.8 ± 1.4
Periumbilical skinfold (mm)	6.0 ± 1.9	6.3 ± 2.3	5.6 ± 1.2*
Suprailliac skinfold (mm)	4.7 ± 2.1	5.1 ± 2.7	4.3 ± 0.8*
Body fat (%)	9.9 ± 3.8	10.2 ± 4.3	9.5 ± 2.9

+$p < 0.1$; *$p < 0.05$; ***$p < 0.001$ (based on *t*-test).

9.9% also characterizes a lean population. When comparing the two sub-populations, waist circumference as well as suprailliac and periumbilical skin folds are significantly greater among settled males suggesting greater abdominal fat reserves compared to the nomadic males despite the lack of difference in overall %BF.

Figure 1 shows the frequencies of AR CAG repeats by residence. Overall, the number of CAG repeats ranges from 15 to 34, with a median of 22.5 and an overall average of 22.6 ± 3.1. Settled and nomadic males show no difference in either the median (23 for both groups) or average length of CAG repeats (22.6 ± 2.9 vs. 22.7 ± 3.4; $p = 0.70$ by testosterone test).

Table 2 shows anthropometric values by AR CAG repeat length <=20 and >20. Men with shorter AR CAG repeat length exhibit a significantly greater waist circumference and WHR ratio. None of the other anthropometric measures differ between the two groups.

Table 3 shows the result of analyses of the relationship of AR CAG repeat and age-related testosterone. Neither Am nor Pm testosterone shows a significant association with AR GAG length (split at CAG = 20), or a significant interaction between AR GAG length and age.

Table 4 shows the results of multivariate analyses of body composition testing for the predicted interaction between Pm testosterone and AR CAG repeat length. Pm testosterone is a significant positive predictor for all the variables except height and AMPBA, both of which show

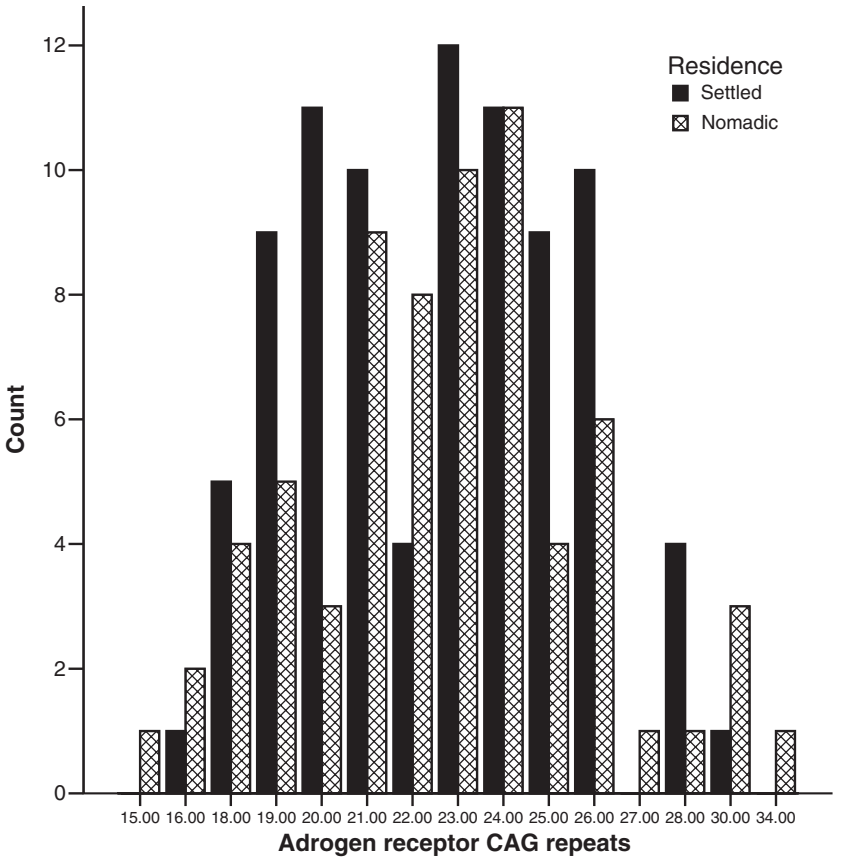

Figure 1 Frequency of CAG repeats among Ariaal Men. The frequency of repeats ranges from 15 to 34 within the range of 11 to 34 established as normal in a US population.

Table 2 Body composition by androgen receptor CAG repeat length among Ariaal males

Variable	<=20	>20
N	41	115
Age (years)		
Height (cm)t	171.4 ± 6.6	172.8 ± 6.6
Weight (kgs)	53.6 ± 8.0	52.7 ± 6.8
Body mass index (wt/ht2)	18.2 ± 1.9	17.6 ± 1.9
Arm circumference (mm)	23.3 ± 1.7	23.1 ± 2.2
Waist circumference (mm)	72.9 ± 7.1	70.4 ± 5.3*
Hip circumference (mm)	86.3 ± 5.5	86.4 ± 5.1
Waist hip ratio (WHR)	0.84 ± 0.05	0.81 ± 0.04***
Subscapular skinfold (mm)	8.0 ± 2.5	7.4 ± 2.4
Midaxillary skinfold (mm)	5.8 ± 2. 3	5.2 ± 1.4
Triceps skinfold (mm)	5.0 ± 1.8	4.8 ± 1.8
Suprailliac skinfold (mm)	5.0 ± 2.5	4.6 ± 1.9
Periumbilical skinfold (mm)	5.9 ± 1. 7	6.0 ± 2.0
Body fat (%)	10.6 ± 4.3	9.6 ± 3.5

*p = 0.05; ***p = 0.001 (based on t-test).

Table 3 Androgen receptor and age related pattern of testosterone

	Am salivary testosterone	Pm salivary testosterone
Adj. r^2	0.16	0.05
Predictor	β	β
Nomadic residence	−.416***	−.265**
Age group	−.105	−.048
AR CAG repeat length	−.038	−.070
AR × age group	−.018	.048

***p < 0.001.

a trend in the same direction. AR CAG repeat length is also a significant positive predictor of height, FFM, %BF, waist circumference and suprailliac skinfold, and shows its trend for BMI. The interaction term Pm testosterone × AR CAG repeat length is a negative significant predictor for all of the variables tested, with the exception of AMPBA. The negative sign of the β-coefficient means that men with shorter CAG repeats show a stronger relationship between Pm testosterone and body composition.

Discussion

The results presented here are of interest in three ways. First, they indicate a greater number of AR CAG repeats among the Ariaal as compared to other African populations for which data is available (Kittles *et al.*, 2001), suggesting greater variation in AR CAG repeats length among African populations than previously recognized. Second, they provide evidence that AR CAG repeat length modulates the impact of testosterone on overall body size and body composition, particularly the adipose tissue. Third, they point to a close association between central adiposity and testosterone as previously reported in western populations (Svartberg *et al.*, 2004). Together these results suggest that the AR plays an important role in modulating energy allocation among men under conditions of energy limitation.

Frequency of CAG repeats

The range of CAG repeats reported here (11–34) is within the normal range of 11–34 established in the US population, whereas CAG repeat number >35 are associated with Kennedy's disease (La Spada *et al.*, 1991). The median of 23 is at the upper limit of the values of 19 to 22 from 13 populations genotyped by Esteban *et al.* (2006). The average CAG repeat number of 22.6 ± 3.1 is also at the upper limit of average values reported for those populations, which range from 19.1 ± 2.4 (Ivory Coast) to 22.6 ± 2.4 (Turkey). The higher average reflects the relatively greater range of the Ariaal values, which include 11 individuals with more than 26 repeats, the highest number reported for the populations studied by Esteban *et al.* (2006). Furthermore, in comparison with results on African-Americans (17.8 ± 3.3), Sierra Leoneans (17.3 ± 2.8), and Nigerians (16.7 ± 4.2) from Kittles *et al.* (2001) the Ariaal

Table 4 Testosterone (T) and androgen receptor (AR) CAG length as predictors of body composition

	Height	BMI[a]	FFM[b]	AMPBA[c]	% BF[d]	Waist[e]	SISK[f]
Adj. r^2	0.01	0.10	0.09	0.01	0.17	0.21	0.15
Predictor	β	β	β	β	β	β	β
Nomadic residence	−.005	−.088	−.064	−.044	−.045	−.175*	−.174*
Age	−.011	−1.39†	−.252	−.124	.314	.103	−.109
Pm T	.323†	.620***	.517***	.329†	.603***	.805***	.455**
AR	.420*	.289†	.383*	.159	.329*	.385*	.760***
Pm T × AR	−.498	−624**	−.618**	−.333	−641***	−.819*	−782***

†p < 0.1; *p < 0.05; **p < 0.01; ***p < 0.001.

[a]body mass index; [b]fat-free mass; [c]arm muscle plus bone area; [d]% body fat; [e]waist circumference; [f]suprailliac skinfold.

value of 22.6 ± 3.1 repeats reflect a substantially higher average.

The basis for the higher range of CAG repeat lengths among the Ariaal is not clear at this point. Given the extreme leanness of Ariaal men, it might reflect a shift in the relative costs and benefits of androgenicity associated with chronic undernutrition. While increased androgenecity may have generally beneficial effects, including increased libido, mood and erectile function (Zitzmann *et al.*, 2006) it may also entail greater energy costs. Chronic undernutrition would increase the consequences of those energy costs for survival, thus relaxing selection for shorter CAG repeat length and leading to a higher average number of CAG repeat values as exhibited by the Ariaal men sampled here. However, it is important to note that the distribution of CAG repeat length reported here is potentially biased by the exclusion of bald men from the sample who are more likely to have short CAG repeat lengths (Ellis *et al.*, 2001), making any such speculations tentative.

Turning to the Ariaal sub-population comparison, the lack of a significant difference in CAG length between nomadic and settled Ariaal males is not unexpected. The two groups separated sometime in the middle of the 20th century (Fratkin, 1998) and still maintain close ties by marriage, leaving relatively little chance for genetic differentiation. Thus, differences in average AR CAG repeat length are unlikely to play a role in sub-groups differences in body composition, though the interaction of AR CAG repeat length and environmental factors, such as caloric availability could play a role.

AR CAG length and age-related testosterone

The lack of an association between AR CAG repeats and testosterone levels is consistent with several earlier reports (Krithivas *et al.*, 1999; Harkonen *et al.*, 2003; Canale *et al.*, 2005). In contrast, the lack of an association between AR CAG repeats and age-related testosterone is contrary to the findings that shorter CAG repeat length is associated with faster age-related decline of testosterone (Krithivas *et al.*, 1999; Walsh *et al.*, 2005). These earlier findings have been interpreted to suggest that men with shorter CAG repeats are more sensitive to the feedback effects of testosterone. Thus our results may simply reflect the relative lack of an age-related decline in testosterone among the Ariaal.

Association of testosterone and AR CAG repeats with body composition

Pm testosterone, AR CAG repeat length and their interaction all showed significant associations with body composition. AR CAG repeat length was significantly and positively related to height, and FFM, consistent with the suggestion that testosterone is important in determining final body size (Lukas *et al.*, 2005). Men with more AR CAG repeats are taller, but there is only a marginal effect of Pm testosterone. This suggests that AR CAG repeat length may mediate the effects of testosterone on pubertal growth. Longer CAG repeats may result in less effective testosterone exposure of long bones thus allowing growth to continue and resulting in greater adult height (Zachmann *et al.*, 1976).

Our finding that CAG repeat length is a significant positive predictor of FFM and %BF is consistent with previous results (Zitzmann *et al.*, 2003; Walsh *et al.*, 2005) as is the significant interaction of CAG repeat length with Pm testosterone in predicting %BF (Lapauw *et al.*, 2007). In addition, the fact that Pm testosterone, but not AR CAG repeat length or their interaction, showed an association with AMPBA is consistent with results showing that testosterone administration in young men increases muscle mass, with no interaction with CAG repeat length (Woodhouse *et al.*, 2003).

On the other hand, the positive association of testosterone and overall adiposity (%BF) and central adiposity (waist circumference) contrasts with results from western samples in which a negative relationship between adiposity and testosterone (Vermeulen *et al.*, 1999; Allan *et al.*, 2006) has been reported. Thus this finding requires further consideration.

Mechanisms linking testosterone and adiposity

The positive relationship between adiposity and testosterone among Ariaal men is consistent with previous reports of a positive association between testosterone and body fat among Ariaal (Campbell *et al.*, 2003) and Turkana (Campbell *et al.*, 2006a) nomads. Both endurance runners and individuals on a low calorie/low protein diet show lower adiposity, insulin and bioavailable testosterone compared to sedentary controls (Fontana *et al.*, 2006).

Furthermore, elite runners show a positive association between abdominal fat and serum testosterone levels (Hetland *et al.*, 1998), similar to the positive association of waist circumference and testosterone reported here and in previous studies (Campbell *et al.*, 2003; Svartberg *et al.*, 2004). Thus both low testosterone levels and their positive association with adiposity exhibited by Ariaal men may reflect their low calorie diet, and low adiposity, as well as highlighting the importance of abdominal adiposity.

Interestingly, Ariaal men with shorter AR CAG repeats exhibit a stronger positive relationship between adipose tissue and current testosterone levels, contrary to

expectations based on the lipolytic effects of circulating testosterone (Herbst & Bhasin, 2004). Instead the impact of AR CAG repeat length on the association of testosterone and adiposity may act through the effects of energy status on testosterone production, perhaps by altering the impact of testosterone feedback at the level of the hypothalamus (Crabbe *et al.*, 2007). Alevizaki *et al.* (2003) report higher oestrogen levels among men with more CAG repeats, suggesting that oestrogen feedback might also be involved.

In terms of energy signals, acute hypoglycaemia, has been related to reduced luteinizing hormone (LH) stimulation and testosterone production in human males (Oltmanns *et al.*, 2001), whereas administration of leptin to acutely fasting men stops the decline in testosterone by maintaining LH stimulation (Chan *et al.*, 2003). Thus to the extent that greater adiposity among Ariaal men is reflected in higher blood glucose and leptin levels, it may also be related to higher testosterone levels. However, contrary to expectation, Bribiescas & Hickey (2006) report an inverse relationship between fat and leptin among Ache males, confounding the expectation of leptin as a clear signal of energy stores among chronically undernourished men.

Population comparison

The Ariaal men sampled here are quite lean with an average body fat of 10%. The extent to which our results linking testosterone, variation in the AR and adiposity can be generalized to other energy-limited populations is unclear. Lukas *et al.* (2004) reported a positive association between salivary testosterone and FFM among 100 Zimbabwean men with an average of 15% body fat, whereas Bribiescas (2005) did not find a significant relationship between testosterone and either BMI or FFM among 17 Ache foragers of Paraguay with an average body fat of 18%. Whether variation in AR CAG repeat length plays a role in inter-population variation in the relationship of testosterone to body composition is an obvious question for future investigations.

Conclusions

Among Ariaal males, the distribution of AR CAG repeat lengths is substantially shifted towards longer alleles as compared to those reported for other African populations for which data are currently available. Furthermore, variation in both testosterone and AR CAG repeat length play a role in body composition among Ariaal males, suggesting the possibility of selection against androgenicity in this population. Our analyses suggest that variation in AR CAG repeat length is more strongly related to adiposity, particularly abdominal adiposity, than to muscle, consistent with earlier findings from western samples. The positive relationship between testosterone and adiposity reported here is consistent with previous findings in nutritionally stressed groups and may reflect a close association between energy status and testosterone production among chronically undernourished populations. More work on energy-stressed populations is called for, to help understand the mechanisms by which variation in the male reproductive axis is related to energy status.

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