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ORIGINAL ARTICLE

Exercise training improves free testosterone in lifelong sedentary aging men

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Abstract

As the impact of high intensity interval training (HIIT) on systemic hormones in aging men is unstudied to date, we investigated whether total testosterone (TT), sex hormone binding globulin (SHBG), free testosterone (free-T), and cortisol (all in serum) were altered following HIIT in a cohort of 22 lifelong sedentary (62 ± 2 years) older men.

As HIIT requires preconditioning exercise in sedentary cohorts, participants were tested at three phases, each separated by six weeks' training; baseline (phase A), following conditioning exercise (phase B), and post-HIIT (phase C). Each measurement phase used identical methods. TT was significantly increased following HIIT (~17%; $P<0.001$) with most increase occurring during preconditioning (~10%; $P=0.007$). Free-T was unaffected by conditioning exercise ($P=0.102$) but was significantly higher following HIIT compared to baseline (~4.5%; $P=0.023$). Cortisol remained unchanged from A to C ($P=0.138$).

The present data indicate a combination of preconditioning and HIIT increases TT and SHBG in sedentary older males, with the HIIT stimulus accounting for a small but statistically significant increase in free-T. Further study is required to determine the biological importance of small improvements in free-T in aging men.

Key words: Exercise · HIIT · SHBG · Steroid · Testosterone

Introduction

Testosterone is a sex steroid hormone with profound influence on various tissue (1-3). The precipitous decline in systemic testosterone with age is well described (4). Additionally, sex hormone binding globulin (SHBG) is positively correlated with age, thereby attenuating the unbound fraction of testosterone, which is available for androgen receptor interactions (4,5). With the age-associated reduction in anabolic hormone production, reductions in cardiorespiratory fitness (6), muscle strength (7), and muscle power (8) are also observed. Furthermore, significant correlations between testosterone and measures of physical performance in older adults have been observed (9).

Whilst improvements in fitness can be achieved with exercise training in older adults (10,11) the potential of aging men to increase systemic testosterone through exercise is poorly understood. Whilst some authors have reported elevated total testosterone (TT) in highly trained older males compared to controls (12), this is not always the case (13). For example, experimental data from our laboratory suggest masters athletes exhibit improved peak oxygen uptake, body composition, and endothelial function compared with age-matched lifelong sedentary aging men, without any difference in TT (14-17). Yet, we demonstrated that a six-week intervention of moderate aerobic exercise increased TT in said group of sedentary older males (11). However, sex hormone binding globulin (SHBG) was increased which rendered bioavailable testosterone (bio-T) and free testosterone (free-T) unaltered compared to pre-training.

High intensity interval training (HIIT) uses small volumes of exercise to bring about disproportionate increases in cardiometabolic health (18). Whilst we have reported lifelong exercise has no influence on basal TT, yet moderate aerobic exercise increases TT in sedentary older males, there is a paucity of data concerning the influence of short-term HIIT

on TT and free-T in older males. Therefore, the purpose of the present investigation was to examine the influence of HIIT, following moderate aerobic conditioning, on androgen status in previously sedentary older males. We hypothesized *a priori* that testosterone would increase following HIIT.

Materials and Methods

Subjects

Following familiarization with experimental procedures and approval to exercise by their general practitioner, participants were enrolled to the study which was approved by the University of the West of Scotland Ethics Committee. Twenty-two sedentary, but otherwise healthy, males (62 ± 2 years, with a stature of 175 ± 6 cm, and body mass of 91 ± 16 kg) participated. Subjects did not participate in any organized exercise program and had not done for >30 years prior to the period of moderate aerobic conditioning. To account for the contribution of conditioning exercise and HIIT, participants were tested at three phases; baseline (phase A), following conditioning exercise (phase B), and post-HIIT (phase C) using identical methods.

Exercise Training

Participants undertook a six-week period of pre-conditioning, consisting of 150 $min \cdot wk^{-1}$ moderate intensity aerobic exercise, in line with the ACSM guidelines for exercise for older adults (19), followed by six weeks of supervised HIIT as previously described (14). Because aging men take longer to recover from a single HIIT session (20), sessions were

performed every five days, for six weeks (nine sessions in total). Each session consisted of 6 x 30 s sprints at 40% peak power output (PPO) interspersed with 3 min active recovery on a cycle ergometer (Wattbike Ltd., Nottingham, UK). Sessions were conducted in groups of between four and six participants and were the sole exercise performed during this time. To allow for comparison with other literature, training intensities were compared with power achieved at VO_{2peak}. Training intensity was 141 + 27% of power at VO_{2peak}.

Body Composition

Stature was measured to the nearest 0.1 cm using a stadiometer (Seca, Birmingham, UK), and body mass and body composition was determined by a multi frequency bioelectrical impedance analyzer (BIA [Tanita MC-180MA Body Composition Analyzer, Tanita UK Ltd.]). GMON software (v1.7.0, Tanita UK Ltd.) was used to determine absolute and relative body fat. Fat free mass (FFM) was calculated by subtracting fat mass from total body mass.

Blood Draws and Analysis

Blood samples were collected 07:00-09:00 h, 48-72 hours following the last exercise session as previously described (21). Serum concentrations of TT, SHBG, and cortisol were measured by electrochemiluminescent immunoassay on the E601 module of the Roche Cobas 6000 (Burgess Hill, West Sussex, U.K.). Inter-assay coefficients of variation (CV) over a six-month period were 4.5%, 2.4%, and 4.2% for TT, SHBG, and cortisol respectively. Free-T was calculated using the Vermueulen equation (22).

Data Analysis

Following confirmation of parametricity by a Shapiro-Wilk test of normality and Levene's test for homogeneity of variance, a one way repeated measures analysis of variance (ANOVA) with *post hoc* Bonferroni correction was used to identify differences between time points. Alpha level was set *a priori* at $P<0.05$, and effect size (Cohen's *d*) was calculated. Data are presented as mean ± standard deviation (SD).

Results

TT, free-T, and cortisol pre- and post-HIIT are displayed in figure 1. TT increased from A to B (13.2 ± 5.5 to 14.6 ± 6.1 $nmol \cdot l^{-1}$ respectively [P=0.007, Cohen's *d*=0.24]) and remained elevated at C compared to A (15.4 ± 6.6 $nmol \cdot l^{-1}$ at phase C [P<0.001, Cohen's *d*=0.36]). SHBG increased following preconditioning (P=0.016, Cohen's *d*=0.10 [42.6 ± 22.0 and 45.0 ± 23.9 $nmol \cdot l^{-1}$ at A and B respectively]) and again following HIIT (P=0.003, Cohen's *d*=0.43 vs. A [45.9 ± 24.6 $nmol \cdot l^{-1}$ at phase C]). Free-T was unchanged after preconditioning (P=0.102, Cohen's *d*=0.22 [6.6 ± 1.9 and 7.0 ± 1.8 $ng \cdot dl^{-1}$ at A and B respectively]), with a small increase following HIIT (7.3 ± 2.1 $ng \cdot dl^{-1}$ at phase C [P=0.023, Cohen's *d*=0.36 vs. A]). There was no difference between free-T at phase B and C (P=0.185, Cohen's *d*=0.16). Cortisol was unchanged from A to B (302 ± 114 and 297 ± 107 $nmol \cdot l^{-1}$ respectively [P=0.849, Cohen's *d*=0.05]), and from A to C (256 ± 86 $nmol \cdot l^{-1}$ at phase C [P=0.138, Cohen's *d*=0.46]).

At phase A, body fat percentage was 24.4 ± 11.6%. Body fat percentage decreased ~1.1% following preconditioning (P=0.006, Cohen's *d*=0.10) and a further ~2.2% following HIIT (P=0.008, Cohen's *d*=0.16) which meant body fat percentage was ~3.3% lower at phase

C than at A (P<0.001, Cohen's *d*=0.28). FFM was 66.7 ± 7.1 kg at baseline and was unchanged following preconditioning (P=0.336, Cohen's *d*=0.06). This was followed by a ~3.0% increase post-HIIT (P=0.005, Cohen's *d*=0.26), which was ~3.6% greater than at baseline (P=0.001, Cohen's *d*=0.32).

**INSERT FIGURE 1 NEAR HERE **

Figure 1: Cortisol (upper panel), total testosterone (middle panel), and free testosterone (lower panel) in a group of lifelong sedentary aging males at baseline (A), following conditioning exercise (phase B), and post-high intensity interval training (phase C). *Denotes significantly different from A (P<0.05). Data are displayed as individual samples and mean ± SD.

Discussion

The main finding of this study is that preconditioning exercise and HIIT improves TT by ~17% in previously sedentary older males, which was maintained post-intervention despite the training volume reduction from ~150 min·wk^{-1} to ~3-6 min·wk^{-1} during the final training phase. In addition, progressive increases at each time point ensured free-T was elevated post-intervention, compared to pre-training. A such, HITT may be a time-efficient non-pharmacological strategy in older males to maintain or increase endogenous testosterone concentrations.

We previously hypothesized that increased TT and SHBG were transient physiological responses to initiation of exercise training, and basal testosterone may return to

161 baseline following prolonged training (11). However, the present study indicates HIIT
162 confers a prolonged elevation in TT compared to pre-training (~17%).

163 Previously, we observed no increase in free-T following six weeks' moderate aerobic
164 training in sedentary older males (11). However, the addition of HIIT stimulated a significant
165 increase in the unbound hormone fraction, compared to moderate aerobic training. This
166 occurred because of the ~5% increase in TT, compared to the ~2% increase in SHBG from
167 phase A to C. As such, it is plausible that testosterone available for androgen receptor
168 interaction was increased post-HIIT, which may partly explain increased FFM.

169 Khoo et al. (23) indicated increased TT (~17%) following 24 weeks' moderate-
170 intensity aerobic exercise in middle-aged (~44 years) obese men. Whilst the present study
171 and Khoo et al. (23) both reported increased TT and SHBG, Lovell et al. (24) reported no
172 change to TT, SHBG, or free-T in an older cohort (~74 years) following resistance or aerobic
173 training. Importantly, participants were moderately active rather than sedentary as was the
174 case in the present study and that of Khoo and colleagues (23). Taken together, the small
175 body of comparable literature indicates that exercise training induces statistically significant,
176 if not biologically or clinically relevant, increases in steroid hormones in sedentary middle to
177 older aged men.

178 That previously sedentary aging males can increase TT following moderate exercise
179 training, and free-T following HIIT, is an encouraging finding. Low testosterone is associated
180 with diminished cognitive function, depression, osteoporosis, and deterioration of muscle
181 function (25). Therefore, the confirmation that exercise can increase serum testosterone is
182 important for medical practitioners because exercise has been proposed as an initial treatment
183 for low testosterone (26).

A limitation to the present investigation is that we utilized a single-arm observational design, rather than a randomized control trial. As such it is difficult to conclude whether changes observed at phase C were the result of HIIT, or merely prolonged exercise intervention (of any modality). Moreover, since participants experienced beneficial alterations to body composition, it is feasible that the indirect effect of lower body fat may have resulted in increased free-T, rather than being purely the result of HIIT.

In conclusion, because preconditioning exercise increased both TT and SHBG, only a small increase in free-T was observed, which did not reach significance. However, the combination of preconditioning and HIIT appears a sufficient stimulus to improve free-T in lifelong sedentary aging men. Further study is required to confirm these findings and establish the biological significance of small improvements in free-T in aging men.

Declaration of Interest

Authors declare they have no declaration of interest.

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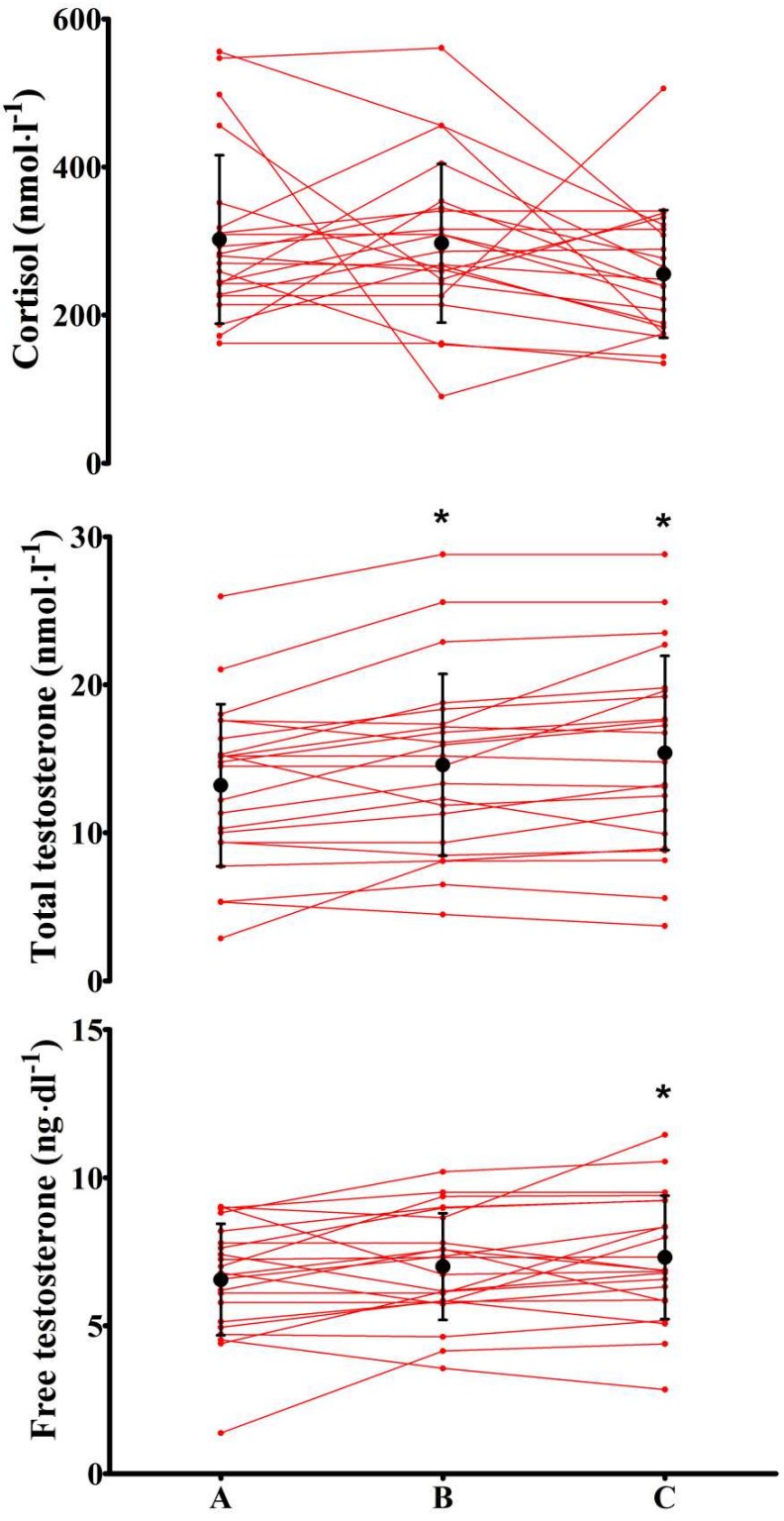
Figure Legends

Figure 1: Cortisol (upper panel), total testosterone (middle panel), and free testosterone (lower panel) in a group of lifelong sedentary aging males at baseline (A), following conditioning exercise (phase B), and post-high intensity interval training (phase C). *Denotes significantly different from A ($P<0.05$). Data are displayed as individual samples and mean ± SD.


Cortisol (nmol·l-1)
600
400
200
0
Total testosterone (nmol·l-1)
30
20
10
0
*
*
Free testosterone (ng·dl-1)
15
10
5
0
*
A
B
C