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Effects of resistance training on testosterone metabolism in younger and older men

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ABSTRACT

This study investigated the effects of resistance training (RT) on the metabolism of testosterone (T) in younger ($n = 5$, 28 ± 3 yrs.) and older ($n = 8$, 70 ± 2 yrs.) men. Experimental heavy resistance exercises (5×10RM leg presses) were performed before and after a 12-month of RT. No age differences were found in the production or metabolic clearance rate of T (determined by stable isotope dilution method), skeletal muscle androgen receptor content or serum LH concentrations due to acute or chronic RT. The T production capacity response to gonadotropin stimulation and the concentrations of the urinary T metabolites (androsterone and etiocholanolone) were lower in the older compared to younger men ($p < 0.05$–0.01). This study further showed that RT may have acute effect on T production and clearance rates, while the exercise-induced increases in serum T appeared to be induced by decreased metabolic clearance rate of T. Attenuated T production capacity and urinary excretion of T metabolites in older men may reflect the known reduction in testicular steroidogenesis upon aging. No changes were observed in T metabolism due to RT indicating a homeostatic stability for this hormone in men of different ages.

1. Introduction

In men, levels of testosterone (T) gradually decrease from age 30 (Feldman et al., 2002) and low T concentrations are associated with low skeletal muscle mass (Baumgartner et al., 1999; Iannuzzi-Sucich et al., 2002). The age-related loss of skeletal muscle mass and function represents increasing risks for physical disability and metabolic disorders in older persons. Resistance training (RT) is one of the most promising interventions to counteract the age-related muscle decline (Dela and Kjaer, 2006). We have previously shown that the acute resistance exercise-induced responses in serum T may change during long-term RT, and the changes could be related to size changes of the trained muscles (Ahtiainen et al., 2003). This finding suggests that acute changes in serum T may have a role in the RT-induced adaptations of skeletal muscles and that T metabolism may change during long-term RT, possibly by transient exercise-induced alterations in T metabolism. However, the effects of RT on T metabolism in aged men have not yet been investigated in detail.

Previous studies have shown that constant infusion of stable isotope-labeled T, combined with T analysis with liquid or gas chromatography–tandem mass spectrometry provides valid measurements of the production rate (PR_T) and metabolic clearance rate of T (MCR_T) upon physiological interventions (Vierhapper et al., 1997; Wang et al., 2004). In men, PR_T is maintained by the feedback regulatory system of the hypothalamic–pituitary–testicular (HPT) axis. The hypothalamus releases in pulsatile fashion gonadotrophin-releasing hormone (GnRH), which in turn stimulates the synthesis and release of luteinizing hormone (LH) from the anterior pituitary gland, which subsequently stimulates T production in testicular Leydig cells. With aging, serum T concentrations progressively decline, by about 1% per year (Harman et al., 2001), mainly due to a decline in the capacity of aging Leydig cells to produce T in response to LH stimulation (Chen et al., 2009). The functional capacity of the HPT axis can be assessed by exogenous

Abbreviations: T, testosterone; PR_T, production rate of testosterone; MCR_T, metabolic clearance rate of testosterone; HPT-axis, hypothalamic–pituitary–testicular axis; GnRH, gonadotrophin-releasing hormone; LH, luteinizing hormone; SHBG, serum sex-hormone binding globulin.

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GnRH or human chorionic gonadotropin (hCG; an analogue of pituitary LH) stimulation tests. Previously it has been shown that acute and chronic endurance training suppresses T responses to GnRH and hCG (Hackney et al., 2003; Kujala et al., 1990; Safarinejad et al., 2009; Vasankari et al., 1993). However, the effects of aging and RT on the HPT axis have not been examined.

The main component of MCR_T is the extensive enzymatic conversions of T in the liver and elimination of T metabolites, such as androsterone and etiocholanolone, by the kidney (Pozo et al., 2010). Thus, urinary androsterone and etiocholanolone can be considered the final end products in the T degradation pathway. The MCR_T processes include also, to a smaller extent, aromatization of T to estradiol (Longcope et al., 1969) and interaction of T with target tissues via androgen receptors (ARs) (Heemers and Tindall, 2007). Changes in AR content determine for the most part the magnitude of the target cell response to T, and therefore down- or up-regulation of AR may be crucial in determining the effects of T upon target tissues. The effects of aging and RT for T metabolism and skeletal muscle AR content are largely unknown.

We hypothesize that regular resistance exercises with possible chronic stimulation of the HPT axis during the long-term RT may induce adaptations in T synthesis and metabolism. Since aging affects serum T concentrations (Vermeulen, 2000), we also hypothesized that the expected RT-induced acute and chronic responses in T metabolism may be attenuated in older compared to younger men and, therefore, may explain possible aging-induced interference in muscular adaptations to long-term RT (Welle et al., 1996). Thus, the purpose of the present study was to examine acute and chronic RT-induced responses on serum T and LH, MCR_T and PR_T, urine androsterone and etiocholanolone, skeletal muscle ARs and testicular production capacity of T (determined by stimulation tests of the HPT-axis with GnRH and hCG), as well as their associations with the muscular adaptations to RT, in younger and older men.

2. Materials and methods

2.1. Subjects

The intervention group consisted of healthy untrained young adult (~25–30 yrs) and older men volunteers (~70–75 yrs). The present study was a part of larger research project whereof the subjects were randomized to the current investigation. The subjects were recruited by advertisements in the local newspaper. Subjects with a background in systematic physical training during the year before the study were excluded. The subject's health status was screened by a physician before inclusion in this study. More detailed medical screening was used for the older men including resting electrocardiogram. Exclusion criteria included cardiovascular and pulmonary diseases, malfunctions of the thyroid gland, diabetes, obesity (body mass index > 30), or any other disease that may have precluded the ability to perform the exercise training and testing. Exclusion criteria included also medications known to influence the endocrine system, heart rate and cardiovascular or neuromuscular performance. The subjects who passed the baseline physical examination were accepted to the study. In accordance with the Declaration of Helsinki, all subjects were carefully verbally informed about the possible risks and benefits of the study and all subjects signed a written consent form before participation in the study. The ethics committees of the University of Jyväskylä (October 24th 2006) and the Central Finland Health Care District approved the study (K-S shp:n Dnro 58/2006).

2.2. Experimental design

The study groups consisted of 9 younger and 9 older men. After the pre-measurements, four younger men withdrawn from the study due to low back pain (n = 1), work-related injury (n = 1), an unknown reason (n = 1) and change of residence (n = 1), and one older man deceased of natural cause. Thus, the final experimental groups consisted of 5 younger (YM; age 28 ± 3 yrs) and 8 older men (OM; age 70 ± 2 yrs).

The subjects were familiarized with all physical performance testing procedures prior to the study. The experimental variables were measured in four separate measurement sessions before and after the 12-month experimental resistance training (RT) period; 1) basal total and free testosterone concentration and anthropometrics in fasting conditions, 2) muscle strength and size, 3) T production and clearance rates, urine excretion of T metabolites, serum LH concentration, and muscle AR protein concentration and 4) HPT-axis stimulation tests. Timetable of the measurements during experimental heavy resistance exercise performed before and after RT is presented in Fig. 1. All pre-measurements were performed 1–2 weeks before the RT and post-measurements were performed within a week following the last training session. To minimize variability in the measures, the subjects were asked to refrain from any strenuous physical activity for at least three days before the measurements and maintain a similar activity and dietary behavior pattern each time. Furthermore, all measurements were always performed at the same time of day to exclude the effects of diurnal variations.

2.3. Resistance training program

Subjects participated in a supervised progressive RT program for 12-months. The present experimental RT program was designed to increase muscle mass and strength extensively throughout the training period according to the recommendations of RT programming for healthy adults (American College of Sports Medicine, 2009; Garber et al., 2011). Leg press, squat and knee extension and flexion exercises were performed for the lower extremity muscles. Four to five other exercises were performed for the other main muscle groups of the body (e.g. bench press, triceps pushdown, lateral pull-down, sit-up, elbow flexion). The training program consisted of whole body RT sessions two times a week during months 1–6. During the first month the training was carried out with light loads (40–60% of one repetition maximum; 1RM) but with multiple 10–20RM sets and with short rest periods between the sets to familiarize to resistance exercises and to improve strength endurance of trained muscles. Then the loads increased progressively up to 60–80% of the 1RM (8–12RM per sets) with a relatively short recovery time between the sets to increase muscle mass. After three months the training program included also higher loads (70–90% of the 1RM) with a longer recovery time between the sets using 5–10RM loads to optimize gains in maximal strength of trained muscles while still increasing muscular hypertrophy. The training program included also two sets performed with lower loads (40–50% of the 1RM with 8–12 repetitions) and higher movement velocities to improve muscle power. At months 7–12, the training program consisted of RT sessions three times per week, with upper and lower body training sessions in turn. All training sessions were supervised by the research team to make sure that proper techniques and progression in the training loads were used in each exercise.

2.4. Experimental heavy resistance exercise

To examine possible changes in acute exercise-induced responses due to long-term RT, the experimental heavy resistance exercise (HRE) sessions were performed before and after the 12-month RT. After the training period, the HRE was performed 3–4 days after the last training session to adapt the recovery time similar to the exercise frequency used during RT. The HRE protocol was hypertrophic in nature and comprised five sets of 10 repetition maximum (10RM) sets of bilateral leg presses (David 210, David Fitness and Medical Ltd., Finland) from a knee angle of 70° to 180° (= leg straight) with a two-minute recovery between the sets.

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