Eur J Appl Physiol (2000) 82: 83–90

ORIGINAL ARTICLE

Tomasz Kostka · Laurent M. Arsac · Marie C. Patricot
Sophie E. Berthouze · Jean-René Lacour
Marc Bonnefoy

Leg extensor power and dehydroepiandrosterone sulfate, insulin-like growth factor-I and testosterone in healthy active elderly people

Accepted: 29 December 1999

Abstract We examined the association between quadriceps muscle function and serum levels of dehydroepiandrosterone sulphate (DHEAS), insulin-like growth factor I (IGF-I) and testosterone in a group of healthy elderly people. Fifty-three independent, community-dwelling elderly subjects (26 men and 27 women) aged from 66 to 84 years volunteered to participate in the study. Physical activity (PA) was evaluated by a questionnaire. Quadriceps maximal muscle power ($\dot{W}_{max}$) and optimal shortening velocity (v_{opt}) were measured on a friction-loaded non-isokinetic cycle ergometer. The $\dot{W}_{max}$ is expressed in relation to body mass ($\dot{W}_{max/kg}$, $W \cdot kg^{-1}$), and in relation to the mass of the two quadriceps muscles ($\dot{W}_{max/Quadr}$, $W \cdot kg_{Quadr}^{-1}$). In women, when adjusted for age, anthropometric measurements and PA indices, IGF-I correlated significantly with $\dot{W}_{max/kg}$ (partial correlation: $r = 0.59$; $P = 0.001$), $\dot{W}_{max/Quadr}$ ($r = 0.58$; $P = 0.002$) and v_{opt} ($r = 0.53$; $P = 0.004$), whereas DHEAS was correlated significantly with $\dot{W}_{max/kg}$ ($r = 0.54$; $P = 0.003$) and $\dot{W}_{max/Quadr}$ ($r = 0.58$; $P = 0.002$). No such correlation was found in men. These findings indicate that in healthy elderly women lower values for quadriceps muscle $\dot{W}_{max}$ and v_{opt} are related, independently of age, anthropometric measurements and PA indices, to lower circulating levels of DHEAS and IGF-I.

Key words Ageing · Hormone · Fitness · Exercise · Muscle strength

T. Kostka · M. Bonnefoy
Service de Médecine Gériatrique, Centre Hospitalier Lyon-Sud, 69495 Pierre-Bénite Cedex, Lyon, France

T. Kostka · L. M. Arsac · J.-R. Lacour
Laboratoire de Physiologie – GIP Exercice, Faculté de Médecine de Lyon-Sud, Lyon, France

T. Kostka (✉)
Department of Preventive Medicine, Medical University, Zachodnia 81/83, 90–402 Lodz, Poland
e-mail: am@laser.net.pl;
Tel.: +48-42-6326029; Fax: +48-42-6326029

M. C. Patricot
Laboratoire de Biochimie (Pr A. Revol), Centre Hospitalier Lyon-Sud, Lyon, France

S. E. Berthouze
Département de Rééducation et Réadaptation Fonctionnelles – GIP Exercice, Faculté de Médecine, Université Jean Monnet, Saint-Etienne, France

Introduction

Ageing is connected with a gradual decrease of skeletal muscle mass and function (Aoyagi and Shephard 1992). Decreased muscle strength and power cause gradually impaired functioning, and due to this impairment, many elderly subjects either approach or reach the disability threshold (Guralnik et al. 1995). Loss of muscle mass is caused by age-related atrophy of fibres, loss of fibres and many chronic debilitating diseases (Brooks and Faulkner 1994). Age-related decreases in strength and function are also attributable to changes in neural drive to the muscle (decreases in maximal voluntary activation of the muscle and changes in agonist/antagonist activation/coactivation; Häkkinen et al. 1995, 1996, 1998a). Age-related decreases in muscle mass and function may also occur as a result of decreasing levels of habitual physical activity (Brooks and Faulkner 1994).

Recently, three hormonal systems have raised an increasing interest due to their potential anabolic effect on muscle function in older subjects. Plasma levels of dehydroepiandrosterone (DHEA) and its sulphate (DHEAS), growth hormone (GH), insulin-like growth factor (IGF)-I, luteinizing hormone/follicle stimulating hormone, and testosterone decline with ageing (Vermeulen et al. 1972; Häkkinen and Pakarinen 1993; Lamberts et al. 1997; Häkkinen et al. 1998b; Kraemer et al. 1998; Proctor et al. 1998; Kraemer et al. 1999). DHEAS, IGF-I and testosterone share some biological activites that counteract the ageing processes: increase in fat-free mass, decrease in adipose tissue and globally increased fitness and well being (Lamberts et al. 1997; Proctor

et al. 1998). Several studies conducted so far in the elderly do not give an unequivocal answer as to the efficacy of hormone replacement strategies in improving muscle function (Rudman et al. 1990; Morley et al. 1993; Holloway et al. 1994; Morales et al. 1994; Thompson et al. 1995; Morales et al. 1998). However, the majority of studies has dealt only with men and has assessed the muscle mass and strength (force) as an index of muscle function. Most habitual daily activities require power (i.e. force as well as some speed of movement). Ageing is associated with a slowing of contraction (Davies et al. 1986; Vandervoort and McComas 1986; Harridge et al. 1997) and a decrease in the optimal shortening velocity (v_{opt}) in the muscles of the lower limb (Kostka et al. 1997; Bonnefoy et al. 1998a). The loss of explosive force production and muscle power is greater and more closely related to age-related physical disability than is the decrease of muscle strength (Bosco and Komi 1980; Clarkson et al. 1981; Häkkinen and Pakarinen 1993; Young and Skelton 1994; Häkkinen et al. 1995, 1996; Thelen et al. 1996; Izquierdo et al. 1999). To date, there are several reports that have assessed muscle function in relation to the plasma levels of selected circulating anabolic hormones in older subjects (Craig et al. 1989; Häkkinen and Pakarinen 1993, 1994, 1995; Häkkinen et al. 1998b; Kraemer et al. 1998, 1999). There are no studies in which DHEAS, IGF-I and testosterone levels have been investigated in relation to both maximal muscle power ($\dot{W}_{max}$) and v_{opt}. Therefore, the current study was designed to examine the association of quadriceps muscle $\dot{W}_{max}$ and v_{opt} with DHEAS, IGF-I and total testosterone (TT) levels in healthy elderly men and women.

Methods

Subjects

Fifty-three independent, community-dwelling elderly subjects aged from 65 to 84 years were recruited as described previously (Bonnefoy et al. 1998b). All of the volunteers were free from ischaemic heart disease, severe aortic stenosis, hypertrophic obstructive cardiomyopathy, osteoarthritis, hepatic or renal failure and any other chronic or evolutive disorder. In addition, subjects who where on hormonal treatment or any other treatment that could influence the measurements to be performed in the study were excluded. The study was approved by an Ethics Committee (Comité Consultatif de Protection des Personnes de la Recherche Biomédicale, Lyon, Centre Léon Bérard) and written informed consent was obtained from all of the subjects.

Protocol

The subjects reported to the laboratory at 1400 hours on 2 consecutive days. They were asked to fast after breakfast, which was taken at 0900 hours. On the 1st day, the physical activity (PA) questionnaire was completed, anthropometric measurements taken and blood samples for hormone determinations collected. Although the blood samplings were taken at 1400 hours, our data are representative, since the circadian variation of IGF-I is minimal in young and old people, and that of DHEAS and testosterone is blunted in the elderly population (Bremner et al. 1983; Liu et al. 1990). On the 2nd day, the subjects performed a quadriceps explosive power test (also at 1400 hours).

Physical activity

The Questionnaire d'Activité Physique Saint-Etienne (QAPSE) has been described previously, and has been validated in a population of healthy elderly subjects (Bonnefoy et al. 1996). It reports retrospectively the activities over 1 week, including the weekend. QAPSE was completed for all of the participants by the same interviewer. In the study presented here, the following QAPSE activity indices were calculated and used for further comparisons:

1. Mean habitual daily energy expenditure (MHDEE).
2. Sports activity index (daily energy expenditure corresponding to leisure time sports activities with intensity levels ranging between 4 and 7 metabolic equivalents).

All QAPSE activity indices are expressed in $kJ \cdot day^{-1}$, and relative to body mass ($kJ \cdot day^{-1} \cdot kg^{-1}$).

Anthropometric data

Anthropometric data were collected by standard methods. Skinfold measurements were taken at four sites: triceps, biceps, subscapula and supraileum. The percentage of body fat was estimated from the skinfold measurements according to the method of Durnin and Womersley (1974). Thigh muscle plus bone volume was calculated using the thigh length, three circumferences measured with a tape, and two skinfold measurements (Jones and Pearson 1969). Quadriceps muscle mass was calculated from a regression equation derived from autopsy studies (Andersen and Saltin 1985). This anthropometric approach was validated against computer-assisted tomography (Saltin 1985), and may have lead to an overestimation of the active quadriceps mass in the elderly in comparison between younger and older subjects. However, the influence on the relationships between quadriceps muscle mass and other parameters within the group of older subjects appears to have been minor. The term "quadriceps' mass" is used in the present study and denotes the sum of the masses of two quadriceps muscles.

Explosive power testing

Mechanical measurements were performed on a friction-loaded cycle ergometer (Monark type 818E, Stockholm, Sweden), as described previously (Arsac et al. 1996; Kostka et al. 1997; Bonnefoy et al. 1998a). Briefly, the ergometer was instrumented with a strain gauge (Interface MFG type, Scottsdale, Ariz., USA) and with an incremental encoder (Hengstler type RIS IP50, 100 pts/turn, Aldingen, Germany) for measurement of the friction force applied by the tension of the belt that surrounds the flywheel, and the flywheel displacement, respectively. The strain gauge was calibrated with a known mass (2.553 kg). Flywheel inertia was calculated using the method proposed by Lakomy (1986). Thus, the acceleration balancing load was added to the friction load for force computations. Instantaneous pedalling velocity (v), force (F) and power output ($\dot{W}$) were calculated every 5 ms and then averaged over each downstroke period. For all experiments, the saddle height was adjusted for each subject and toe clips were removed to prevent any pulling action of the contralateral leg. The subjects were first familiarised with the ergometer by performing 5 min of submaximal cycling at 30–60 W and sprints of 3–4 s against different friction loads. After stretching and a 5-min rest the subjects were asked to perform two 8-s sprints from a standardised starting position. Each sprint was separated by at least 5 min of rest. Friction loads were $0.25 N \cdot kg^{-1}$ and $0.45 N \cdot kg^{-1}$ of body mass. At the signal given by the investigator, the subjects were asked to pedal as fast as possible until told to stop (after 8 s). During the effort, each subject was encouraged vigorously. One sprint provided as many F-v-$\dot{W}$ combinations as pedal downstrokes (about 20). The v-$\dot{W}$ combi-

nations obtained during the two sprints were fitted by a least-square mathematical procedure to establish the v-$\dot{W}$ relationship. The highest value of $\dot{W}$ ($\dot{W}_{max}$) and velocity at maximal power (v_{opt}) were calculated from a third-order polynomial function. $\dot{W}_{max}$ is expressed in relation to body mass ($\dot{W}_{max/kg}$, $W \cdot kg^{-1}$), and to the mass of two quadriceps muscles ($\dot{W}_{max/Quadr}$, $W \cdot kg_{Quadr}^{-1}$). v_{opt} is expressed as pedal revolutions per minute (rpm).

Laboratory analysis

Subjects did not engage in physical exercise for at least 36 h before laboratory measurements. DHEAS, IGF-I and testosterone assays were performed by radioimmunological methods. For DHEAS, we used an Immunotech kit with monoclonal antibody-coated tubes and ^{125}I-labelled DHEAS. The sensitivity of the technique was found to be 0.2 mmol $\cdot$ l^{-1}, and the inter-assay variability was 7.8% at the mean level of 4.7 mmol $\cdot$ l^{-1}. The intra-assay accuracy test, carried out according to the instructions of manufacturer, is less than 10%. IGF-I was determined by an immunoradiometric assay (Ciba-Corning Diagnostics) using ^{125}I-labelled anti-IGF-I and anti-IGF-I monoclonal antibody-coated tubes. The samples were extracted by HCl/ethanol prior to the assay, in order to remove IGF binding proteins. The sensitivity of the method is 0.1 nmol $\cdot$ l^{-1}, and the inter-assay variability is 9.18% at the mean level of 7.6 mmol $\cdot$ l^{-1}. TT was tested with an Immunotech kit. This kit used ^{125}I-labelled testosterone and anti-testosterone antibody-coated tubes. Prior to the assay, samples were extracted by ethyl ether and chromatographed on a Celite column. The sensitivity of the method is 0.1 nmol $\cdot$ l^{-1}, and the inter-assay variability is 7.9% at the mean level of 4.57 nmol $\cdot$ l^{-1}. Cortisol concentration was determined by an automated immunoassay system using the fluorescence polarisation of TDx system (Abbott). The inter-assay variability was 15.3, 9.1 and 11% at the mean levels of 80, 589 and 977 nmol $\cdot$ l^{-1}, respectively. Testosterone:cortisol (T:C) and DHEAS:cortisol (DHEAS:C) ratios were also calculated.

Statistical analysis

Data were verified for normality of distribution and equality of variances. The one-way analysis of variance (ANOVA) and Mann-Whitney test were used to compare gender groups. DHEAS values were normalised using a log transformation for the purpose of statistical analyses; however, results are reported in standard units. Pearson product moment correlations were used to determine the relationships between ergometer measurements and hormone levels. To control the effects of age, anthropometric characteristics and PA indices, a multiple regression analysis was performed and partial correlations were calculated between the residual values of ergometer measurements and residual values of hormone levels. Results are presented as means (SD). The limit of statistical significance was set at $P = 0.05$ for all analyses.

Results

Table 1 gives the demographic and anthropometric characteristics, QAPSE activity indices, ergometer measurements and hormone levels for the study group. There was no age difference between the men and women. The men had higher values for body mass, and quadriceps mass, and the women had a higher percentage of body fat. PA indices in men and women were similar. The men produced higher ergometer measurement values. The hormone levels in men and women were similar for IGF-I and cortisol, and different for DHEAS, TT and T:C ratio (as would be expected).

Table 1 Mean (SD) age, selected anthropometric characteristics, Questionnaire d'Activité Physique Saint-Etienne (*QAPSE*) activity indices, ergometer measurements and hormone levels in men and women. (*DHEAS* dehydroepiandrosterone sulphate, *IGF-I* insulin-like growth factor I; *T:C* testosterone:cortisol ratio, *DHEAS:C* DHEAS:cortisol ratio, *MHDEE* mean habitual daily energy expenditure, $\dot{W}_{max}$ maximum muscle power, v_{opt} optimum velocity of contraction, $\dot{W}_{max/kg}$ $\dot{W}_{max}$ relative to body mass, $\dot{W}_{max/Quadr}$ $\dot{W}_{max}$ relative to quadriceps' muscle mass, *Sports act*. sports activity index)

Characteristics	Men (n = 26)	Women (n = 27)
Age (years)	71.0 (4.2)	70.6 (3.8)[a]
Body mass (kg)	75.9 (12.4)	63.4 (9.0)***
Body fat (%)	25.2 (5.1)	34.4 (3.6)***
Quadriceps mass (kg)	4.00 (0.64)	3.15 (0.42)***
MHDEE/kg ($kJ \cdot kg^{-1} \cdot day^{-1}$)	132.9 (23.5)	126.1 (19.9)
Sports act./kg ($kJ \cdot kg^{-1} \cdot day^{-1}$)	16.5 (10.6)	13.1 (11.0)[a]
$\dot{W}_{max/kg}$ ($W \cdot kg^{-1}$)	6.67 (0.98)	4.23 (1.16)***
$\dot{W}_{max/Quadr}$ ($W \cdot kg_{Quadr}^{-1}$)	126.9 (23.0)	83.9 (18.4)***
v_{opt} (rpm)	96.8 (9.0)	74.7 (10.0)***
IGF-I (nmol $\cdot$ l^{-1})	18.81 (7.83)	17.94 (9.00)
DHEAS (μmol $\cdot$ l^{-1})	2.91 (2.20)	1.66 (1.21)*
Testosterone (nmol $\cdot$ l^{-1})	19.98 (7.25)	0.91 (0.49)[a] ***
Cortisol (nmol $\cdot$ l^{-1})	334.8 (98.5)	315.9 (158.0)
T:C ratio (1000)	61.35 (18.38)	3.38 (2.51)[a] ***
DHEAS:C ratio (1000)	9.23 (7.90)	6.09 (5.19)

*$P < 0.05$; ***$P < 0.001$ for the difference
[a] Mann-Whitney test

Table 2 Correlation coefficients for ergometer measurements with hormone levels in women (n = 27) (*IGF-I* insulin-like growth factor I)

Variable	$\dot{W}_{max/kg}$ ($W \cdot kg^{-1}$)	$\dot{W}_{max/Quadr}$ ($W \cdot kg_{Quadr}^{-1}$)	v_{opt} (rpm)
IGF-I (nmol $\cdot$ l^{-1})	0.52**	0.59***	0.69***
DHEAS (μmol $\cdot$ l^{-1})	0.50**	0.70***	0.47*
Testosterone (nmol $\cdot$ l^{-1})	0.13	0.06	0.02
Cortisol (nmol $\cdot$ l^{-1})	0.08	0.08	0.06
T:C ratio (1000)	−0.14	−0.22	−0.17
DHEAS:C ratio (1000)	0.27	0.45*	0.29

*$P < 0.05$; **$P < 0.01$; ***$P < 0.001$

Table 3 Correlation coefficients for ergometer measurements with hormone levels in men (n = 26)

Variable	$\dot{W}_{max/kg}$ ($W \cdot kg^{-1}$)	$\dot{W}_{max/Quadr}$ ($W \cdot kg_{Quadr}^{-1}$)	v_{opt} (rpm)
IGF-I (nmol $\cdot$ l^{-1})	0.004	−0.08	0.21
DHEAS (μmol $\cdot$ l^{-1})	0.20	0.15	0.12
Testosterone (nmol $\cdot$ l^{-1})	0.01	−0.01	0.04
Cortisol (nmol $\cdot$ l^{-1})	−0.29	−0.35	−0.14
T:C ratio (1000)	0.27	0.33	0.16
DHEAS:C ratio (1000)	0.19	0.17	−0.03

Tables 2 and 3 show the Pearson product moment correlation coefficients between ergometer measurements and hormone levels in the women and men, respectively. In the women, all three ergometer measurements correlated positively with IGF-I and DHEAS. A positive relationship was also obtained

between $\dot{W}_{max/Quadr}$ and DHEAS:C ratio in the female group. No such correlation could be found for the men.

A multiple regression model that controlled for the effects of age, body mass, percentage of body fat, quadriceps' muscle mass and PA indices revealed significant relationships between the ergometer measurements and hormone levels for the women. IGF-I correlated significantly with $\dot{W}_{max/kg}$ (partial correlation: $r = 0.59$; $P = 0.001$), $\dot{W}_{max/Quadr}$ ($r = 0.58$; $P = 0.002$) and v_{opt} ($r = 0.53$; $P = 0.004$; see Fig. 1), whereas DHEAS was correlated with $\dot{W}_{max/kg}$ ($r = 0.54$; $P = 0.003$) and $\dot{W}_{max/Quadr}$ ($r = 0.58$; $P = 0.002$; see Fig. 2). Again, no such correlation could be found for the men.

Discussion

The aim of this study was to examine simultaneously the relationship of DHEAS, IGF-I and testosterone levels with quadriceps muscle function in healthy elderly men and women. The major finding is that in healthy women aged >65 years, circulating DHEAS and IGF-I levels in the serum are related, independently of age, anthropometric characteristics and habitual PA, to the variances of the $\dot{W}_{max}$ and v_{opt} of the quadriceps muscles. Quadriceps muscles play a basic role in the common activities of daily living like walking or rising from a chair. Lower-extremity function deteriorates more rapidly with age than in the upper limbs (Aoyagi and Shephard 1992). Since knee weakness is strongly correlated to the occurrences of falls and disability in the elderly (Guralnik et al. 1995), preserving quadriceps power may be considered to be one of the most important determinants of functional independence in older people.

Information on the relationship between muscle function and anabolic hormone profile stems from cross-sectional data, studies investigating acute hormone responses to resistance exercise, and prospective studies assessing the influence of resistance training and hormone replacement therapy. Lower DHEAS levels were recorded in elderly women with functional limitation (Instrumental Activities of Daily Living) and confinement, with a trend towards the same correlations in elderly men (Berr et al. 1996). In addition, Ravaglia et al. (1996) found the lowest functioning levels in older men with the lowest DHEAS levels. No association between muscle strength and IGF-I levels was found in older men (Papadakis et al. 1995) or women (Boonen et al. 1998). In a recent study by Kiel et al. (1998), no correlation was observed between muscle strength and circulating IGF-I among older persons with functional limitations. Häkkinen and Pakarinen (1993) found positive correlations between individual values of maximal strength and explosive force production of the leg extensor muscles and circulating testosterone and testosterone/sex-hormone binding globulin (SHBG) ratio in middle-aged and older women. The authors concluded that the decreasing basal level of blood testosterone that occurs over the years in ageing people, especially in females, may lead to the decreasing anabolic effects on muscles having an association with age-related declines in the maximal voluntary neuromuscular capacity in ageing people.

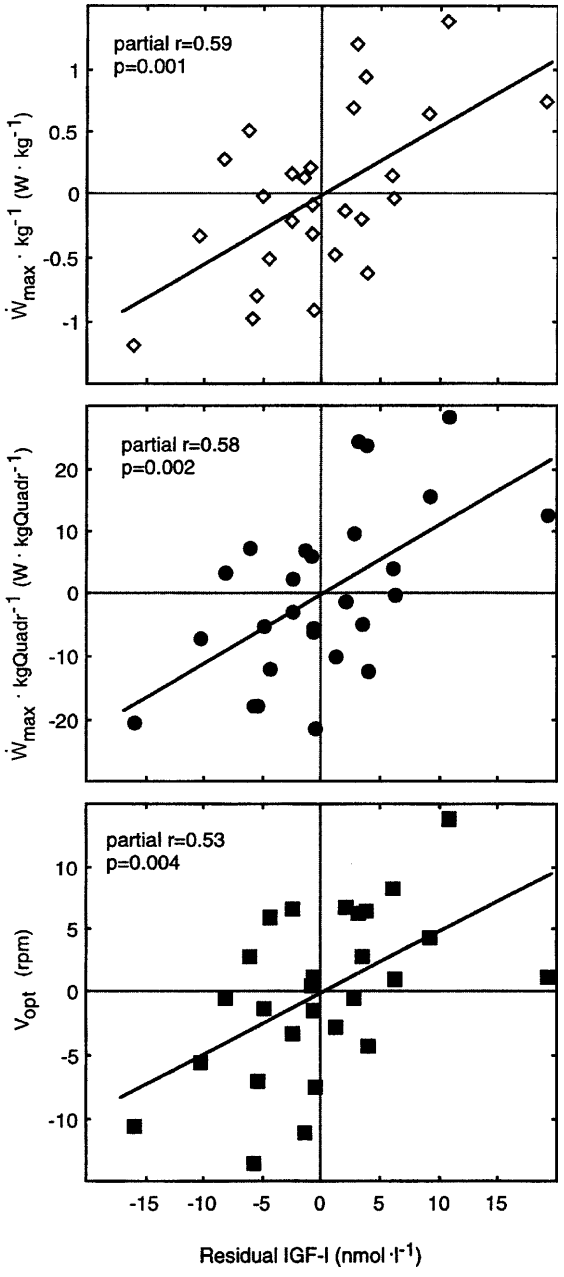

Fig. 1 Partial correlation between insulin-like growth factor (IGF)-I and maximal muscle power expressed in relation to both body mass and quadriceps' muscle mass ($\dot{W}_{max/kg}$, $\dot{W}_{max/Quadr}$), respectively, and v_{opt} after adjustment for age, body mass, percentage of body fat, quadriceps' muscle mass and PA indices in women ($n = 27$). For both variables, the residuals are the difference between the observed value and that predicted from its correlation with age, body mass, percentage of body fat, quadriceps' muscle mass and PA indices

Several studies have assessed the influence of resistive exercise on anabolic hormone levels in older subjects. In

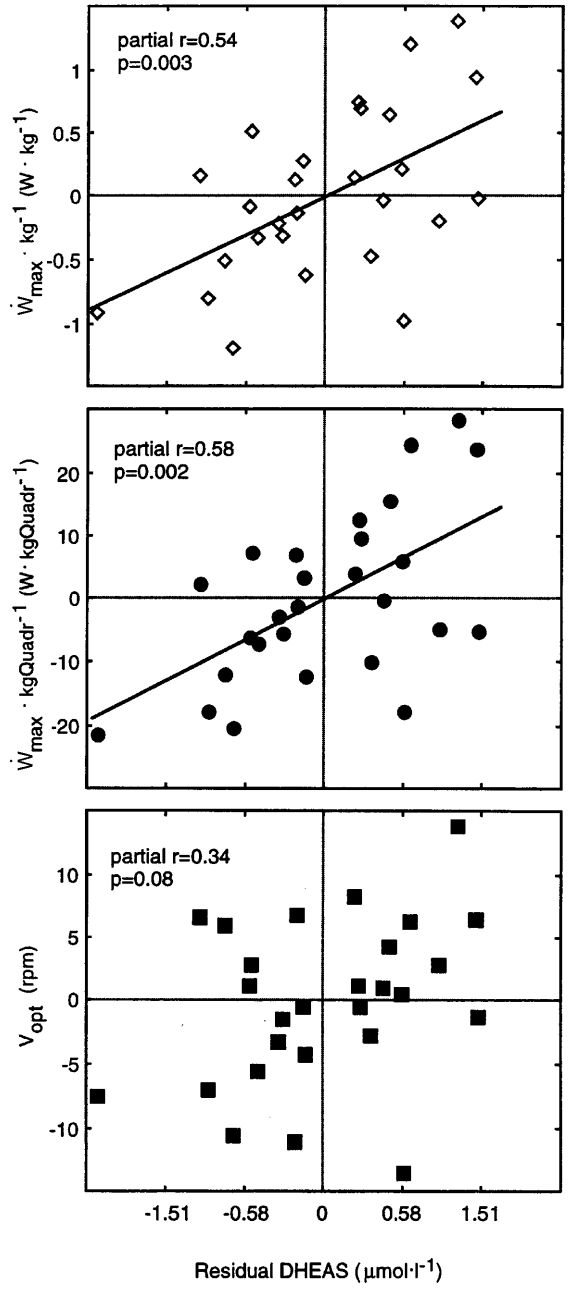

Fig. 2 Partial correlation between DHEAS and $\dot{W}_{max/kg}$, $\dot{W}_{max/Quadr}$ and v_{opt} after adjustment for age, body mass, percentage of body fat, quadriceps' muscle mass and PA indices in women ($n = 27$)

general, the magnitude of anabolic hormone responses is dependent upon: (1) the volume and intensity of exercise used, (2) the recovery period between the sets, (3) the amount of muscle mass involved in exercise action, and (4) the age and gender of the subject (Craig et al. 1989; Häkkinen and Pakarinen 1995; Häkkinen et al. 1998b; Kraemer et al. 1998). Acute heavy-resistance exercise increases TT in older men, although to a lesser extent than in younger individuals (Häkkinen et al. 1998b; Kraemer et al. 1998). Lower-intensity resistive effort seems to have no influence on testosterone levels in elderly subjects (Craig et al. 1989).

The effects of resistance training on basal levels of hormones have been examined in several studies. IGF-I increased slightly during 24 weeks of resistance training in a group of eight elderly men (Taaffe et al. 1994). On the other hand, 16 weeks of progressive resistive exercise training did not affect plasma IGF-I levels in men aged 50–70 years (Niclas et al. 1995), and 12 weeks of progressive resistance training caused no significant decrease in basal testosterone levels in 63-year-old men (Craig et al. 1989). Following a 12-week progressive, strength-training experiment involving older men and women, no systematic changes were observed in the mean concentrations of TT, free testosterone, cortisol, SHBG, T:C or T:SHBG (Häkkinen and Pakarinen 1994). However, the individual levels of TT, the T:C ratio, and the individual changes in strength during the last 4, most intensive training weeks, gave a significant positive linear correlation. In a recent study of Kraemer et al. (1999), after 10 weeks of heavy resistance training, older men demonstrated a significant increase in TT in response to exercise stress, along with significant decreases in resting TT.

The possible contribution of DHEAS, IGF-I and testosterone deficits to altered body composition and decreased muscle function in age-advanced subjects has provided a rationale for recent clinical trials with hormone-replacement therapy. Several studies have found favourable changes in body composition in response to recombinant human growth hormone (Rudman et al. 1990; Holloway et al. 1994), recombinant human IGF-I (Thompson et al. 1995) and DHEA (Morales et al. 1994). These changes, however, were accompanied by significant negative side effects. Morales et al. (1998) observed gender dimorphic responses after 6 months of treatment with a 100-mg dose of DHEA in 50- to 65-year-old subjects. An increase in the serum DHEAS:C ratio and IGF-I was observed in both genders, but fat body mass decreased and muscle strength increased in the men ($n = 8$), while total body mass increased in the women ($n = 8$). An increase in muscle strength was observed in old hypogonadal males receiving testosterone replacement therapy (Morley et al. 1993).

Taken together, the results of the studies conducted so far indicate that resistance training in the elderly does not lead to apparent changes in the concentrations of anabolic hormones. If observable, the response to resistive training is different from that in younger individuals, is less drastic, and may be gender-specific. Similarly, studies conducted so far in the elderly do not give an unequivocal answer as to the efficacy of hormone-replacement strategies in improving muscle function.

In the present study we have extended previous observations to all three major anabolic hormonal systems in both elderly men and women. The major finding of this study seems to contrast with some previous studies, which did not find any relationship between muscle strength and circulating IGF-I in older women. This discrepancy may be explained by the fact that we used $\dot{W}_{max}$ as an index of muscle function. High correlations

obtained for both $\dot{W}_{max/kg}$ (the capacity to move a body from place to place) as well as $\dot{W}_{max/Quadr}$ and v_{opt} (indices of the physiological properties of quadriceps muscles) suggest that both overall and intrinsic power is associated with circulating DHEAS and IGF-I levels in older women. Although no muscle biopsy samples were taken in the present study, our data suggest that in older women, DHEAS and IGF-I levels may be related to muscle composition (percentage of fast-twitch fibres). A slowing of v_{opt} reflects a change in muscle quality (a decrease in the proportion of type IIb fibres; Hautier et al. 1996). v_{opt} has not yet been assessed in relation to circulating anabolic hormones. The strong relationship between v_{opt}, and DHEAS and IGF-I may tempt one to speculate that the atrophying effects of age on fast-twitch fibres may be lesser in older women with higher circulating levels of DHEAS and IGF-I. A similar relationship of $\dot{W}_{max}$ and v_{opt}, to DHEAS and IGF-I may also explain why the relationship between muscle strength (as the second component of $\dot{W}_{max}$, beside v_{opt}) and IGF-I was less visible in previous studies.

The lack of correlation between muscle function and hormones in men is in accord with the majority of previous studies. However, some trend towards a negative relationship with cortisol and a positive relationship with the T:C ratio should be noted. This may reflect the hormonal regulation of muscle hypertrophy that has been described in animals (Crowley and Matt 1996) and observed in younger men (Busso et al. 1990). The T:C ratio and DHEAS:C ratio have been proposed to be useful indicators of anabolic/catabolic balance (Busso et al. 1990; Morales et al. 1998). The T:C ratio is known to be correlated with muscular force, and is used for the monitoring of resistance training (Alén et al. 1988). Further studies with larger samples of elderly subjects should clarify this problem.

The gender difference observed in the relationship of DHEAS and IGF-I levels with quadriceps muscle function is worthy of interest. Our data, together with those of previous reports, suggest that in older men the cortisol concentration, probably together with testosterone, is a better predictor of muscle function than DHEAS or IGF-I. Increasing testosterone concentration (or T:C ratio) increases skeletal muscle synthesis and strength, probably mediated by the stimulation of the intramuscular IGF-I system (Urban et al. 1995). The physiologically low concentration of testosterone in women may induce compensative stimulation of the growth hormone/IGF-I axis in response to an increase in physical work, in order to enhance muscle protein synthesis. Another explanation may be that in older women, a positive influence of exercise on IGF-I production is mediated by DHEAS (Bonnefoy et al. 1998b), resulting in a very similar relationship between muscle function measurements, and serum levels of both DHEAS and IGF-I.

Other factors can also interfere with the association between muscle function and circulating hormones. Age-related decreases in muscle strength and power may also be due to decreased voluntary neural drive to muscles and to specific changes in agonist activation and antagonist coactivation (Häkkinen et al. 1995, 1996, 1998a). Neural adaptations seem to play a great role in explaining strength and power gains during resistance training in the elderly (Häkkinen et al. 1998a). Furthermore, strength training can induce changes at the receptor level, not necessarily influencing blood androgen levels (Deschenes et al. 1994).

In conclusion, the results of the present study suggest that in older women, the lower quadriceps muscle $\dot{W}_{max}$ and v_{opt} may reflect lower circulating levels of DHEAS and IGF-I. The results obtained are limited to a group of healthy, elderly subjects. The cross-sectional character of the study also limits data interpretation. Further longitudinal studies should address the role of the hormonal milieu and resistance training as potential modulators of muscle function deterioration with age.

Acknowledgements T.K. was supported by a grant from Hospices Civils de Lyon and by a grant 502-11-449 from Medical University of Lodz.

References

Alén M, Pakarinen A, Häkkinen K, Komi PV (1988) Responses of serum androgenic-anabolic and catabolic hormones to prolonged strength training. Int J Sports Med 9: 229–233

Andersen P, Saltin B (1985) Maximal perfusion of skeletal muscle in man. J Physiol (Lond) 366: 233–249

Aoyagi Y, Shephard R (1992) Aging and muscle function. Sports Med 14: 376–396

Arsac LM, Belli A, Lacour JR (1996) Muscle function during brief maximal exercise: accurate measurements on a friction-loaded cycle ergometer. Eur J Appl Physiol 74: 100–106

Berr C, Lafont S, Debuire B, Dartigues J, Baulieu E (1996) Relationship of dehydroepiandrosterone sulfate in the elderly with functional, psychological, and mental status, and short-term mortality: a French community-based study. Proc Natl Acad Sci 93: 13410–13415

Bonnefoy M, Kostka T, Berthouze SE, Lacour J-R (1996) Validation of physical activity questionnaire (QAPSE) in healthy elderly volunteers. Eur J Appl Physiol 74: 528–533

Bonnefoy M, Kostka T, Arsac LM, Berthouze SE, Lacour J-R (1998a) Peak anaerobic power in elderly men. Eur J Appl Physiol 77: 182–188

Bonnefoy M, Kostka T, Patricot MC, Berthouze SE, Mathian B, Lacour J-R (1998b) Physical activity and dehydroepiandrosterone sulfate, insulin-like growth factor-I and testosterone in healthy active elderly people. Age Ageing 27: 745–751

Boonen S, Lysens R, Verbeke G, Joosten E, Dejaeger E, Pelemans W, Flamaing J, Bouillon R (1998) Relationship between age-associated endocrine deficiencies and muscle function in elderly women: a cross-sectional study. Age Ageing 27: 449–454

Bosco C, Komi PV (1980) Influence of aging on the mechanical behaviour of leg extensor muscles. Eur J Appl Physiol 45: 209–219

Bremner W, Vitiello M, Prinz P (1983) Loss of circadian rhythmicity in blood testosterone levels with aging in normal men. J Clin Endocrinol Metab 56: 1278–1281

Brooks S, Faulkner J (1994) Skeletal muscle weakness in old age: underlying mechanisms. Med Sci Sports Exerc 26: 432–439

Busso T, Häkkinen K, Pakarinen A, Carasso C, Lacour J-R, Komi PV, Kauhanen H (1990) A systems model of training responses and its relationship to hormonal responses in elite weight-lifters. Eur J Appl Physiol 61: 48–54

Clarkson PM, Kroll W, Melchionda AM (1981) Age, isometric strength, rate of tension development and fiber type composition. J Gerontol 36: 648–653

Craig BW, Brown R, Everhart J (1989) Effects of progressive resistance training on growth hormone and testosterone levels in young and elderly subjects. Mech Ageing Dev 49: 159–169

Crowley MA, Matt KS (1996) Hormonal regulation of skeletal muscle hypertrophy in rats: the testosterone to cortisol ratio. Eur J Appl Physiol 73: 66–72

Davies C, Thomas D, White M (1986) Mechanical properties of young and elderly human muscle. Acta Med Scand [Suppl] 711: 219–226

Deschenes MR, Maresh CM, Armstrong LE, Covault J, Kraemer WJ, Crivello JF (1994) Endurance and resistance exercise induce muscle fiber type specific responses in androgen binding capacity. J Steroid Biochem Mol Biol 50: 175–179

Durnin JV, Womersley J (1974) Body fat assessed from total body density and its estimation from skinfold thickness: measurements on 481 men and women aged from 16 to 72 years. Br J Nutr 32: 77–97

Guralnik JM, Ferrucci L, Simonsick EM, Salive ME, Wallace RB (1995) Lower-extremity function in persons over the age of 70 years as a predictor of subsequent disability. N Engl J Med 332: 556–561

Häkkinen K, Pakarinen A (1993) Muscle strength and serum testosterone, cortisol, and SHBG concentrations in middle-aged and elderly men and women. Acta Physiol Scand 148: 199–207

Häkkinen K, Pakarinen A (1994) Serum hormones and strength development during strength training in middle-aged and elderly males and females. Acta Physiol Scand 150: 211–219

Häkkinen K, Pakarinen A (1995) Acute hormonal responses to heavy resistance exercise in men and women at different ages. Int J Sports Med 16: 507–513

Häkkinen K, Pastinen UM, Karsikas R, Linnamo V (1995) Neuromuscular performance in voluntary bilateral and unilateral contraction and during electrical stimulation in men at different ages. Eur J Appl Physiol 70: 518–527

Häkkinen K, Kraemer WJ, Kallinen M, Linnamo V, Pastinen UM, Newton RU (1996) Bilateral and unilateral neuromuscular function and muscle cross-sectional area in middle-aged and elderly men and women. J Gerontol Biol Sci 51: B21–29

Häkkinen K, Kallinen M, Izquierdo M, Jokelainen K, Lassila H, Mälkiä E, Kraemer WJ, Newton RU, Alen M (1998a) Changes in agonist-antagonist EMG, muscle CSA, and force during strength training in middle-aged and older men. J Appl Physiol 84: 1341–1349

Häkkinen K, Pakarinen A, Newton RU, Kraemer WJ (1998b) Acute hormone responses to heavy resistance lower and upper extremity exercise in young versus old men. Eur J Appl Physiol 77: 312–319

Harridge S, Magnusson G, Saltin B (1997) Life-long endurance-trained elderly men have high aerobic power, but have similar muscle strength to non-active elderly men. Aging Clin Exp Res 9: 80–87

Hautier C, Linossier M, Belli A, Lacour J, Arsac L (1996) Optimal velocity for maximal power production in non-isokinetic cycling is related to muscle fibre type composition. Eur J Appl Physiol 74: 114–118

Holloway L, Butterfield G, Hintz R, Gesundheit N, Marcus R (1994) Effects of recombinant human growth hormone on metabolic indices, body composition, and bone turnover in healthy elderly women. J Clin Endocrinol Metab 79: 470–479

Izquierdo M, Aguado X, Gonzalez R, López JL, Häkkinen K (1999) Maximal and explosive force production capacity and balance performance in men of different ages. Eur J Appl Physiol 79: 260–267

Jones P, Pearson J (1969) Anthropometric determination of leg fat and muscle plus bone volumes in young male and female adults. J Physiol (Lond) 204: 63P–66P

Kiel DP, Puhl J, Rosen CJ, Berg K, Murphy JB, MacLean DB (1998) Lack of association between insulin-like growth factor-I and body composition, muscle strength, physical performance or self-reported mobility among older persons with functional limitations. J Am Geriatr Soc 46: 822–828

Kostka T, Bonnefoy M, Arsac L, Berthouze S, Belli A, Lacour J-R (1997) Habitual physical activity and peak anaerobic power in elderly women. Eur J Appl Physiol 76: 81–87

Kraemer WJ, Häkkinen K, Newton RU, McCormick M, Nindl BC, Volek JS, Gotshalk LA, Fleck SJ, Campbell WW, Gordon SE, Farrell PA, Evans WJ (1998) Acute hormonal responses to heavy resistance exercise in younger and older men. Eur J Appl Physiol 77: 206–211

Kraemer WJ, Häkkinen K, Newton RU, Nindl BC, Volek JS, McCormick M, Gotshalk LA, Gordon SE, Fleck SJ, Campbell WW, Putukian M, Evans WJ (1999) Effects of heavy-resistance training on hormonal response patterns in younger vs. older men. J Appl Physiol 87: 982–992

Lakomy HKA (1986) Measurements of work and power output using friction-loaded cycle ergometers. Ergonomics 29: 509–517

Lamberts SWJ, van der Beld AW, van der Lely A-J (1997) The endocrinology of aging. Science 278: 419–424

Liu C, Laughlin G, Fischer U, Yen S (1990) Marked attenuation of ultradian and circadian rhythms of dehydroepiandrosterone in postmenopausal women: evidence for a reduced 17,20-desmolase enzymatic activity. J Clin Endocrinol Metab 71: 900–906

Morales A, Nolan J, Nelson J, Yen S (1994) Effects of replacement dose of dehydroepiandrosterone in men and women of advancing age. J Clin Endocrinol Metab 78: 1360–1367

Morales AJ, Haubrich RH, Hwang JY, Asakura H, Yen SSC (1998) Effects of six-month treatment with a 100-mg daily dose of dehydroepiandrosterone (DHEA) on circulating sex steroids, body composition and muscle strength in age-advanced men and women. Clin Endocrinol 49: 421–432

Morley J, Perry H, Kaiser F, Kraenzle D, Jensen J, Houston K, Mattammal MHP Jr (1993) Effects of testosterone replacement therapy in old hypogonadal males: a preliminary study. J Am Geriatr Soc 41: 149–152

Niclas BJ, Ryan AJ, Treuth MM, Harman SM, Blackman MR, Hurly BF, Rogers MA (1995) Testosterone, growth hormone and IGF-I responses to acute and chronic resistive exercise in men aged 50–70 years. Int J Sports Med 16: 445–450

Papadakis MA, Grady D, Tierney MJ, Black D, Wells L, Grunfeld C (1995) Insulin-like growth factor 1 and functional status in healthy older men. J Am Geriatr Soc 43: 1350–1355

Proctor DN, Balagopal P, Nair KS (1998) Age-related sarcopenia in humans is associated with reduced synthetic rates of specific muscle proteins. J Nutr 128 [Suppl 2]: 351S–355S

Ravaglia G, Forti P, Maioli F, Boschi F, Bernardi M, Pratelli L, Pizzoferrato A, Gasbarrini G (1996) The relationship of dehydroepiandrosterone sulfate (DHEAS) to endocrine-metabolic parameters and functional status in the oldest-old. Results from an Italian study on healthy free-living over-ninety-years-olds. J Clin Endocrinol Metab 81: 1173–1178

Rudman D, Feller AG, Nagaraj HS, Gergans GA, Lalitha PY, Goldberg AF, Schlenker RA, Cohn L, Rudman IW, Mattson DE (1990) Effects of human growth hormone in men over 60 years old. N Engl J Med 323: 1–6

Saltin B (1985) Hemodynamic adaptations to exercise. Am J Cardiol 55: 42D–47D

Taaffe DR, Pruitt L, Reim J, Hintz RL, Butterfield G, Hoffman AR, Marcus R (1994) Effect of recombinant human growth hormone on the muscle strength response to resistance exercise in elderly men. J Clin Endocrinol Metab 79: 1361–1366

Thelen DG, Schultz AB, Alexander NB, Ashton-Miller JA (1996) Effects of age on rapid ankle torque development. J Gerontol Med Sci 51: M226–M232

Thompson JL, Butterfield GE, Marcus R, Hintz RL, van Loan M, Ghiron L, Hoffman AR (1995) The effects of recombinant human insulin-like growth factor-I and growth hormone on body composition in elderly women. J Clin Endocrinol Metab 80: 1845–1852

Urban RJ, Bodenburg YH, Gilkison C, Foxworth J, Coggan AR, Wolfe RR, Ferrando A (1995) Testosterone administration to elderly men increases skeletal muscle strength and protein synthesis. Am J Physiol 269: E820–E826

Vandervoort A, McComas A (1986) Contractile changes in opposing muscles of the human ankle joint with aging. J Appl Physiol 61: 361–367

Vermeulen A, Rubens R, Verdonck L (1972) Testosterone secretion and metabolism in male senescence. J Clin Endocrinol 34: 730–735

Young A, Skelton DA (1994) Applied physiology of strength and power in old age. Int J Sports Med 15: 149–152