Effects of Strength Training on Muscle Strength, Cross-Sectional Area, Maximal Electromyographic Activity, and Serum Hormones in Premenopausal Women with Fibromyalgia

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ABSTRACT. ***Objective.*** To examine the effects of strength training on basal concentrations and acute responses of serum hormones, and their possible interrelationships with training induced muscle hypertrophy and strength gains of the knee extensor muscles in women with fibromyalgia (FM) and healthy controls.

Methods. Twenty-one premenopausal women with FM were randomized to 21 week strength training (FMT; n = 11) or control (FMC; n = 10) groups. Twelve premenopausal sedentary healthy women served as controls (HC). Surface electromyographic (EMG) activity, maximal unilateral isometric force of the right knee extensors, and muscle cross-sectional area (CSA) of the quadriceps femoris throughout the lengths of 3/12 to 12/15 of the femur (Lf) were measured. Serum concentrations of total and free testosterone and growth hormone (GH) were analyzed at rest and in pre- and post-exercise conditions, while levels of insulin-like growth factor and dehydroepiandrosterone sulfate were measured at rest only.

Results. Mean (SD) maximal force increased by 18% (10%) ($p < 0.001$) in the FMT group, and by 22% (12%) ($p < 0.001$) in the HC, while in the FMC it remained unchanged. Maximum integrated EMG of the agonists (VL + VM/2) increased in HC by 22% ($p < 0.05$) and in the FMT by 19% ($p < 0.05$). Significant increases in the CSA of the QF were observed at 5 to 12/15 Lf in FMT ($p < 0.05$–0.01) and at 3 to 12/15 Lf in HC ($p < 0.05$–0.001), while in FMC the CSA remained unchanged. No training induced changes occurred in the basal concentrations of serum hormones examined. A significant acute increase took place in the mean concentration of GH at pre-training in HC ($p < 0.01$) and in the FMT ($p < 0.05$), while at post-training the elevations after the loading ($p < 0.001$ and 0.05) remained elevated up to 15 min ($p < 0.05$) in HC and up to 30 min ($p < 0.01$) post-loading in the FMT.

Conclusion. Both the magnitude and time course of adaptations of the neuromuscular system to resistance training in women with FM were completely comparable to those taking place in healthy women. Basal levels of the anabolic hormones seem to be similar in women with FM compared to age matched healthy women. Observations recorded during the acute loading conditions might be considered an indication of the training induced adaptation of the endocrine system, showing that the acute GH response may become systematic after strength training in both women with FM and controls. (J Rheumatol 2002;29:1287–95)

Key Indexing Terms:
SERUM HORMONES MUSCLE CROSS-SECTIONAL AREA
STRENGTH FIBROMYALGIA STRENGTH TRAINING

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Since most prominent symptoms in fibromyalgia (FM) are localized to peripheral soft tissue, especially to muscles, numerous studies have been carried out to find out abnormalities in muscle structure[1,2] and function[3,4] in these patients. Some studies have described decreased voluntary muscle strength[5-8], while no differences in muscle strength between patients with FM and healthy subjects were found in some others[3,9,10].

Since growth hormone (GH) and insulin-like growth factor I (IGF-I) impose important influences on muscle growth and strength, and consequently on the trainability capacity of an individual, special interest has been focused on these hormones. The release of GH occurs primarily during stages 3 and 4 of non-REM sleep, which is disturbed in patients with FM[11]. Further, studies in FM have shown low basal levels of GH[12] and IGF-I[11,13], and subsequently, in a placebo controlled randomized study, the symptoms and function of patients with FM improved and lowered serum levels of IGF-I increased with recombinant GH treatment[14].

Dehydroepiandrosterone (DHEA) and its sulfate ester, DHEAS, are steroids that are released from the adrenal glands. DHEAS and DHEA may act as precursors of androgens and estrogens in several tissues, and the local formation of sex steroids may explain part of the effects of DHEA/DHEAS in brain and in peripheral tissues. It has been suggested that DHEA may modulate the receptor activities of several neurotransmitters in nerve tissue. Further decline in circulating DHEA/DHEAS concentrations may associate with neuropsychological consequences, such as impaired memory, cognition, and mood[15] that are also common in FM.

Physical exercise is known to be a powerful intervention to obtain longterm effects on muscle function, but little is known about the physiological trainability of patients with FM. Studies of physical exercise in management of FM have been reviewed by Sim and Adams[16]. However, no study applied intensive strength training and repetitive heavy resistance exercises to investigate the effects of the training on basal concentrations and acute responses of serum anabolic hormones and their possible relationships with training induced muscle hypertrophy and strength gains in patients with FM.

Heavy resistance exercise is a potent stimulus for acute increases in circulating testosterone and GH in younger healthy men, while the responses are lowered in magnitude in elderly men[17-19]. The acute response in these anabolic hormones is lower in women than in men. Further, elderly women may show no response at all[18,20].

Hyposecretion of GH and adrenal androgens have been associated with aging and with poor perceived health[11,21]. Clinical features of FM resemble those described in GH and DHEA/DHEAS deficiencies in adults. Reduced GH and IGF-I concentrations are also associated with reduced muscle mass and strength[22], but the possible association of DHEAS in this respect needs further experimental evidence.

We examined the effects of muscle strength training on basal concentrations and acute responses of serum anabolic hormones in premenopausal women with FM and in matched healthy controls. We also studied the possible interrelationships of hormone levels with training induced muscle hypertrophy and strength gains of the muscles in these women during a prolonged strength training period.

MATERIALS AND METHODS

Subjects. Twenty-one premenopausal women with FM from our outpatient clinic were recruited for study. Before inclusion the patients were examined by a rheumatologist (PH) to confirm the diagnosis of FM according to the 1990 American College of Rheumatology criteria[23]. After inclusion FM patients were randomly allocated to training (FMT; n = 11) or control (FMC; n = 10) groups. Twelve premenopausal sedentary healthy women served as training controls (HC). The physical characteristics of the study groups are presented in Table 1. The subjects in all groups were habitually physically active (such as walking, swimming, biking, skiing), but they had no background in strength training. Two patients from the FMT and one from the FMC group were unemployed and one from FMC retired at the beginning of the followup. All the other subjects were employed.

This work was part of a larger research project, and some results obtained with these subjects have been published[10,24]. However, all the data presented here [serum hormones, isometric strength, electromyographic (EMG) activity of the unilateral knee extension, and muscle cross-sectional area] are unique to this part of the investigation.

Study design. The experimental period of 25 weeks consisted of a 4 week control period followed by a 21 week strength training period. The subjects in the 2 training groups were tested on 5 different occasions using identical protocols. The first month of the study (between the measurements at Week –4 and at 0) served as a control period, when no strength training was carried out, but the subjects maintained their normal low intensity recreational physical activities (e.g., walking, jogging, biking, swimming, and aerobics). Subjects were tested before and after this control period. Thereafter, the FMT and HC subjects started a supervised experimental strength training period for 21 weeks. The measurements were repeated during the strength training period at 7 week intervals (i.e., Weeks 0, 7, 14, and 21). The FMC subjects maintained their normal low intensity recreational physical activities but did not participate in the strength training as the other 2 groups did.

Table 1. Demographic data of the groups (means ± SD) studied: training women with FM (FMT), training healthy controls (HC), and nontraining women with FM (FMC).

	FMT, n = 11	FMC, n = 10	HC, n = 12
Age, yrs	39 (6)	37 (5)	37 (6)
Height, cm	165 (6)	164 (6)	162 (5)
Weight, kg			
Before	70 (10)	72 (16)	63 (8)
After	70 (10)	72 (16)	64 (8)
Percentage fat			
Before	34 (4)	32 (7)	32 (4)
After	33 (4)	32 (7)	31 (5)
Number of tender points			
Before	16 (2)	15 (2)	
After	15 (4)	16 (2)	
Duration of symptoms, yrs	12 (4)	12 (10)	

Muscle strength testing. Maximal unilateral isometric force of the right knee extensors and flexors was measured using a David-200 dynamometer[25] (David Fitness and Medical Ltd., Outokumpu, Finland). The subject was in a seated position with hip and knee joints at 110° and 107° angles, respectively. On command the subjects were instructed to exert their maximal force as fast as possible during a period of 3–4 s. A minimum of 3 trials was completed for each subject and the best result (N) was used for the subsequent statistical analysis.

Electromyographic recordings. EMG activity during the isometric knee extension and flexion actions of the right leg were recorded from the vastus lateralis (VL), vastus medialis (VM), and biceps femoris (BF). Bipolar (20 mm interelectrode distance) surface EMG recording (miniature size skin electrodes, 650437, Beckman) was employed. The electrodes were placed longitudinally on the motor point areas determined by an electrical stimulator. The positions of the electrodes were marked on the skin by small ink tattoos[26]. These dots ensured the same electrode positioning in each test over the 25 week experimental period. EMG signals were recorded telemetrically (2000 Glonner, Biomes). The EMG signal was amplified (by a multiplication factor of 200; low pass cutoff frequency 360 Hz/3 dB^{-1}) and digitized at the sampling frequency of 1000 Hz by an online computer system. EMG was integrated (iEMG) and expressed for 1 s ($\mu V \times s$) for each muscle separately during the maximal peak force phase of the maximal isometric action. The iEMG of the BF acting as an antagonist was also recorded during the isometric knee extension action. To calculate the antagonist coactivation percentage for the BF muscle during the extension action, the following formula was used: iEMG of BF during extension/iEMG of BF during flexion × 100[25,26].

Muscle cross-sectional area (CSA). The muscle cross-sectional area of the right quadriceps femoris was assessed before and after the 21 week strength training using magnetic resonance imaging (MRI) (1.5 Tesla, Gyroscan S15, Philips; Keski-Suomen Magneettikuvaus Ltd., Jyväskylä, Finland). The length of the femur (Lf), taken as the distance from the bottom of the lateral femoral condyle to the lower corner of the femur head, was measured in the coronal plane. Subsequently, 15 axial scans of the thigh interspaced by a distance of 1/15 Lf were obtained from the level of 1/15 to 15/15 Lf[27]. Great care was taken to reproduce the same, individual femur length each time using the appropriate anatomical landmarks. All MR images were then imported to a Macintosh computer for calculation of muscle CSA. For each axial scan, CSA computation was carried out on the quadriceps femoris as a whole and for the final calculation of the CSA, slices 3/15 to 12/15 were used (slice 3 being closer to the knee joint of the thigh). CSA (measured as cm^2) was determined by tracing manually along the border of the quadriceps femoris.

The percentage of fat in the body was estimated from measurements of skinfold thickness from 4 different sites[28].

Blood collection and analyses. Serum samples for the hormonal analyses were kept frozen at –20°C until assayed. Serum testosterone concentrations were measured with the Chiron Diagnostics ACS:180 automated chemiluminescence system using an ACS:180 analyzer (Chiron Diagnostics, Medfield, MA, USA). The sensitivity of the testosterone assay was 0.42 $nmol \cdot l^{-1}$, and the intraassay coefficient of variation was 6.7%. The concentrations of serum-free testosterone and dehydroepiandrosterone sulfate (DHEAS) were measured by radioimmunoassays using kits obtained from Diagnostic Products Corp. (Los Angeles, CA, USA). The sensitivity of the free testosterone assay was 0.52 $pmol \cdot l^{-1}$ and the intraassay variation was 3.8%. The respective values were 0.06 $\mu mol \cdot l^{-1}$ and 4.5% for the DHEAS assay. Concentrations of growth hormone (GH) were measured using radioimmunoassay kits from Pharmacia Diagnostics (Uppsala, Sweden). The sensitivity of the GH assay was 0.2 $\mu g \cdot l^{-1}$ and the intraassay variation was 2.5–5.1%. Serum IGF-I concentrations were measured by radioimmunoassays using reagent kits from DiaSorin Inc. (Stillwater, MN, USA). The method included an ODS-silica extraction procedure for the serum samples. The sensitivity of the IGF-I assay was < 2.0 nmol/l, and the intraassay variation was 9.2%. All samples for each test subject were analyzed in the same assay for each hormone.

Pain and fatigue. General pain and fatigue of FM patients during the preceding one week period at both pre- and post-training tests were assessed on a 100 mm visual analog scale. In fatigue the end descriptions were 0 = no fatigue and 100 = worst possible fatigue.

Experimental strength training. The supervised 21 week strength training program of the FMT and HC subjects was a total body program in a 2 day/week format. Each training session included 2 exercises for the leg extensor muscles: the bilateral leg press exercise and the bilateral and/or unilateral knee extension exercise on the David-200 machine. In addition, each training session included 4 to 5 exercises for the other main muscle groups of the body (the bench press and/or the triceps push-down and/or lateral pull-down exercise for the upper body; the sit-up exercise for the trunk flexors and/or another exercise for the trunk extensors; and the bilateral/unilateral elbow and/or knee flexion exercise and/or leg adduction/abduction exercise). Loads were determined during the training sessions throughout the 21 week training period according to the maximum repetition method.

During the first 7 weeks the subjects trained with loads of 40 to 70% of the one repetition maximum (1 RM). Subjects performed 10–20 repetitions per set and performed 3–4 sets of each exercise. The loads were 40 to 60% and 60 to 70% of the maximum by Week 11 and 40 to 60% and 60 to 80% by Week 14. In the 2 exercises for the leg extensor muscles the subjects now performed either 8–12 repetitions per set (at lower loads) or 5–8 repetitions per set (higher loads) and performed 3–5 sets. In the other 4 exercises the subjects performed 10–12 repetitions per set and performed 3–5 sets. During the last 7 weeks of training (Weeks 14–21), in the 2 exercises for the leg extensor muscles subjects performed 5–8 repetitions per set with loads 70 to 80% of maximum and 8–12 repetitions per set with the loads of 40 to 60% and performed 4 to 6 sets. In the other 4 exercises, 8–12 repetitions per set were performed for 3 to 5 sets altogether. All training sessions included warmup and cooldown exercises using a bicycle ergometer and muscle stretching.

The strength training utilized was a typical heavy resistance training program, but about 20% of the total of the leg extensor exercises (leg press and knee extension) with light loads (40 to 60% of the maximum) was performed according to the principle of explosive strength training. These repetitions were executed as explosively as possible (rapid muscle actions) throughout the range of motion. During the 21 week experimental training period the subjects continued their ordinary daily chores and took part in recreational low intensity physical activities such as walking, jogging, swimming, biking, or gymnastics 1–3 times per week in the manner they were accustomed to before this experiment.

Heavy resistance protocol for examination of acute hormone responses. The heavy resistance protocol at Week 0 before the training period as well as at Week 21 after the 21 week strength training period included the bilateral leg press exercise on a machine (David-210). For the exercise the subject started from the flexed knee position (70°) and extended the knees concentrically to full extension (180°), then lowered the load eccentrically back to the starting position. The actual loads were always the repetition maximums (RM) for each subject so that they performed 10 repetitions per set with the maximal load possible for a total of 5 sets (5 × 10 RM). The recovery time between sets was 2 min. Loads were adjusted during the course of the session due to fatigue so that each subject would be able to perform 10 repetitions at each set. If the load happened to become too heavy, the subject was assisted slightly during the last 1–3 repetitions of the set while she maintained her maximum performance, so that the required number of repetitions could be reached.

Basal blood samples during the 4 week control period and 21 week strength training. To examine the basal concentrations of serum hormones, blood samples were drawn from the antecubital vein of each subject after 10 h of fasting and about 8 h of sleep in the mornings (between 7:30 and 8:30 AM) during the one month control period (at Week –4 and Week 0) as well as during the 21 week training period (at Weeks 7, 14, and 21).

Blood samples during the heavy resistance loading protocol. To examine

acute hormone responses to the heavy resistance loading, blood samples were drawn twice (within 1 h) during the control day at Week 0 and twice (within 1 h) during the second control day after the training at Week 21 from the antecubital vein of each subject. Blood samples were drawn 4 times during the 2 heavy resistance exercise days (pre- and post-loading samples within about 1 h as well as 15 min and 30 min after termination of the training session) at Week 0 and at Week 21. The heavy resistance protocol was performed between 8:00 AM and 6:00 PM, but always at the same time of day for each subject (at the corresponding time of day as the blood sampling during the controls days) before and after the 21 week training period. Subjects were instructed to maintain their normal food intake prior to the heavy resistance exercise protocol and to have their last light meal during that day no later than 2 h before the session.

Statistics. The means, standard deviations (SD), and standard errors (SE) are given as descriptive statistics. To determine the effects of strength training the data were analyzed by multivariate analysis of variance with repeated measures (ANOVA). Probability adjusted t tests were used for pairwise comparison when appropriate. The coefficients of correlation were calculated with the Pearson test. The level of statistical significance was $p < 0.05$.

The Ethics Committee of the University of Jyväskylä granted approval for this study. All subjects gave written informed consent.

RESULTS

The mean (SD) maximal isometric knee extension force of the right leg increased by 18% (10%) ($p < 0.001$) in the FMT group, by 22% (12%) ($p < 0.001$) in HC, while the FMC showed no systematic change by 1% (9%) (nonsignificant) (Figure 1). The corresponding changes in isometric knee flexion forces were 13% (11%) ($p < 0.01$), 26% (18%) ($p < 0.001$), and –2% (15%) (NS) in the FMT, HC, and FMC, respectively (Figure 2). Maximum iEMG of the 2 agonists (VL + VM/2) recorded during the isometric knee extension action increased in HC by 22% ($p < 0.05$) and in FMT by 19% ($p < 0.05$) (iEMG for VL, Figure 3). Maximum iEMG of agonist BF during the knee flexion action increased in the HC by 20% ($p < 0.05$) and in FMT by 13% (NS). The initial antagonist BF coactivation percentages of 21 ± 10% and 23 ± 10% during the extension action remained unaltered in both groups during the 21 week training period.

The cross-sectional area of the quadriceps femoris did not differ between the groups at baseline. The mean (SD) CSA of QF was greatest at 9/15 Lf, being 57.0 (5.0) cm^2 in the FMT, 59.8 (5.5) cm^2 in FMC, and 57.2 (4.7) cm^2 in HC. Statistically significant increases in the CSA of the QF were observed at 5–12/15 Lf in the FMT ($p < 0.05$–0.01) and at 3–12/15 Lf in the HC ($p < 0.05$–0.001) during the 21 week training period, while in FMC the CSA remained statisti-

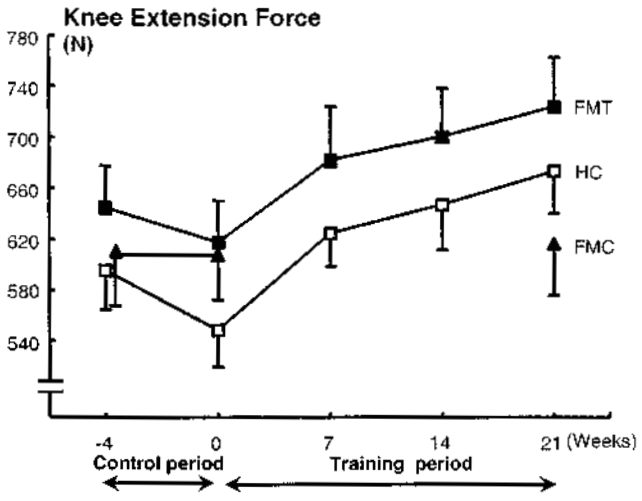

Figure 1. Mean ± SE maximal voluntary isometric force of the right knee extension action in training women with FM (FMT), training healthy female controls (HC), and nontraining female controls with FM (FMC) during the 4 week control period and the 21 week strength training period.

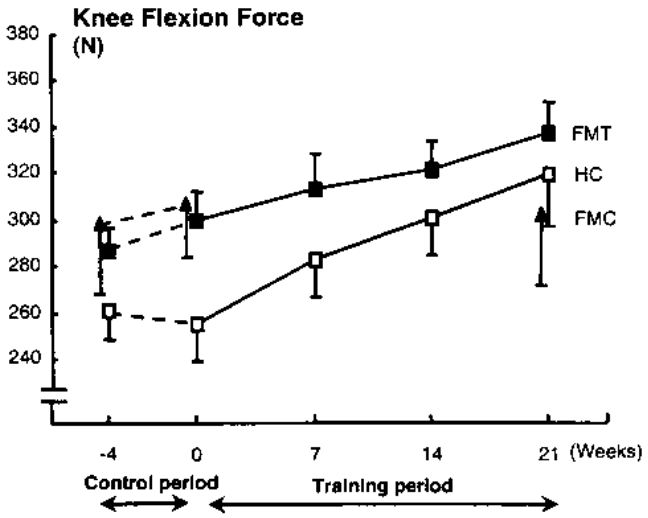

Figure 2. Mean ± SE maximal voluntary isometric force of the right knee flexion action in FMT, HC, and FMC during the 4 week control period and the 21 week strength training period.

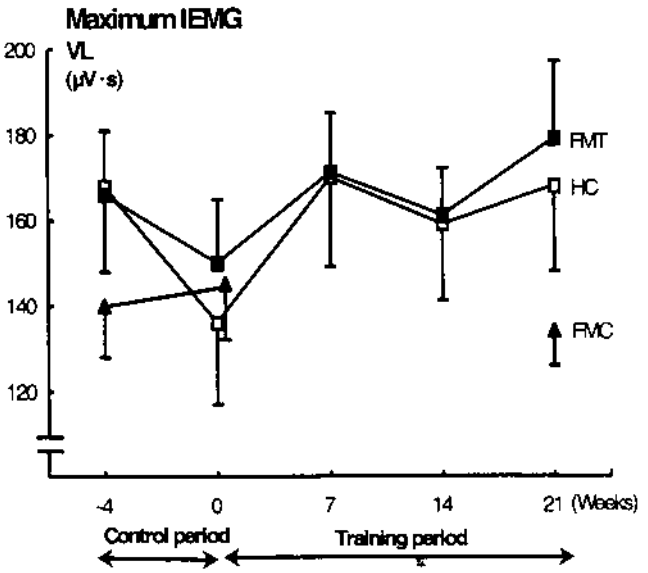

Figure 3. Mean ± SE maximum integrated electromyographic activity (iEMG) of the vastus lateralis muscle (VL) of the right knee extension action in FMT, HC, and FMC during the 4 week control period and the 21 week strength training period.

cally unchanged (Figure 4). The mean relative increases (mean of all Lf) of the QF of 7% for the FMT and 9% for the HC did not differ significantly from each other, but differed ($p < 0.05$) from the 2% (NS) recorded in the FMC.

Table 2 depicts the basal serum hormone concentrations of total testosterone, free testosterone, DHEAS, IGF-I, and GH for the patients and controls at Weeks –4, 0, 7, 14, and 21. No systematic changes in any hormone concentrations were observed in the FMC during the experimental period.

Acute loading. Serum hormone concentrations of testosterone, free testosterone, and GH remained unaltered in FMT and HC during the control days (pre- and post-samples within 1 h) at Week 0 (before training) and at Week 21 (after the 21 week strength training period) (data not shown). No significant changes took place in serum testosterone and free testosterone concentrations during the heavy resistance fatiguing loading either during the pre-training or post-training conditions (Table 3). However, a significant acute increase took place in the mean concentration of GH at pre-training in both the HC ($p < 0.01$) and the FMT ($p < 0.05$) (Figure 5). At post-training the GH concentrations in HC were elevated immediately after the loading ($p < 0.001$) and remained elevated up to 15 min ($p < 0.05$). In the FMT the immediate elevation was also significant ($p < 0.05$) and remained elevated up to 15 min ($p < 0.01$) and up to 30 min ($p < 0.01$) post-loading.

In FMT, pain values before and after the 21 week training period were 48 (25) and 24 (19) mm, respectively. In FMC the corresponding values were 35 (19) and 60 (27) mm. Fatigue decreased from 62 (22) to 43 (25) mm ($p < 0.05$) in FMT. In FMC the fatigue remained unchanged, with a value of 59 (31) mm recorded before and 60 (22) mm after the experimental period.

DISCUSSION

The primary findings confirmed that the 21 week progressive strength training in female patients with FM and healthy women resulted (1) in large and comparable gains in isometric strengths of the knee extensor and flexor muscles. Further, (2) the strength gains were accompanied in both

Table 2. Basal serum hormone concentrations (means ± SD) in FMT, HC, and FMC.

	–4 Weeks	0 Weeks	7 Weeks	14 Weeks	21 Weeks
Testosterone, nmol/l					
FMT	1.2 (0.3)	1.2 (0.5)	1.4 (0.7)	1.3 (0.6)	1.4 (0.8)
FMC	1.7 (0.7)	1.5 (0.7)	—	—	1.7 (0.5)
HC	1.6 (0.5)	1.6 (0.6)	1.3 (0.4)	1.6 (0.8)	1.3 (0.5)
Free testosterone, pmol/l					
FMT	3.9 (2.4)	3.4 (2.1)	4.2 (3.7)	3.8 (2.7)	4.0 (2.8)
FMC	6.8 (4.7)	5.6 (3.4)	—	—	6.0 (3.1)
HC	4.8 (2.7)	5.4 (4.1)	4.8 (3.1)	5.2 (3.6)	4.8 (3.6)
DHEAS, μmol/l					
FMT	3.08 (1.05)	3.18 (1.02)	3.28 (1.72)	3.52 (2.14)	3.22 (1.54)
FMC	3.61 (1.27)	3.19 (1.43)	—	—	3.52 (1.15)
HC	5.22 (3.55)	5.62 (4.19)	5.7 (2.78)	5.21 (3.34)	5.00 (3.60)
IGF-I, nmol/l					
FMT	32.8 (7.5)	36.1 (11.8)	37.1 (9.7)	36.7 (7.9)	32.6 (11.6)
FMC	28.2 (4.9)	28.8 (3.2)	—	—	27.0 (3.5)
HC	26.9 (9.9)	25.6 (8.1)	23.1 (5.0)	23.7 (9.2)	26.1 (9.2)
GH, μg/l					
FMT	1.84 (4.58)	0.85 (1.84)	3.44 (5.77)	2.48 (6.36)	2.09 (4.20)
FMC	1.49 (1.36)	2.38 (2.71)	—	—	1.49 (1.50)
HC	0.85 (0.61)	1.20 (1.86)	2.23 (2.45)	1.54 (2.31)	2.88 (4.96)

Table 3. Serum hormone concentrations (mean ± SD) before and immediately after the single heavy resistance loading session, and after recovery of 15 and 30 min before and after the 21 week strength training period in FMT and HC.

	Heavy Resistance Loading (Pre-Training at Week 0)				Heavy Resistance Loading (Post-Training at Week 21)			
	Before	After	15 min After	30 min After	Before	After	15 min After	30 min After
Testosterone, nmol/l								
FMT	1.0 (0.5)	1.0 (0.3)	1.2 (0.2)	1.2 (0.3)	0.8 (0.4)	0.8 (0.3)	0.9 (0.4)	0.8 (0.4)
HC	1.1 (0.6)	1.1 (0.4)	1.3 (0.4)	1.3 (0.5)	1.0 (0.3)	1.6 (0.7)	1.1 (0.4)	1.0 (0.3)
Free testosterone, pmol/l								
FMT	2.9 (1.8)	3.0 (1.7)	3.4 (1.9)	3.3 (2.0)	2.5 (1.2)	2.8 (1.1)	2.6 (1.2)	2.1 (0.9)
HC	4.2 (2.9)	4.4 (2.8)	4.2 (2.5)	4.4 (2.9)	3.4 (2.7)	4.4 (3.0)	3.9 (3.4)	3.4 (3.2)

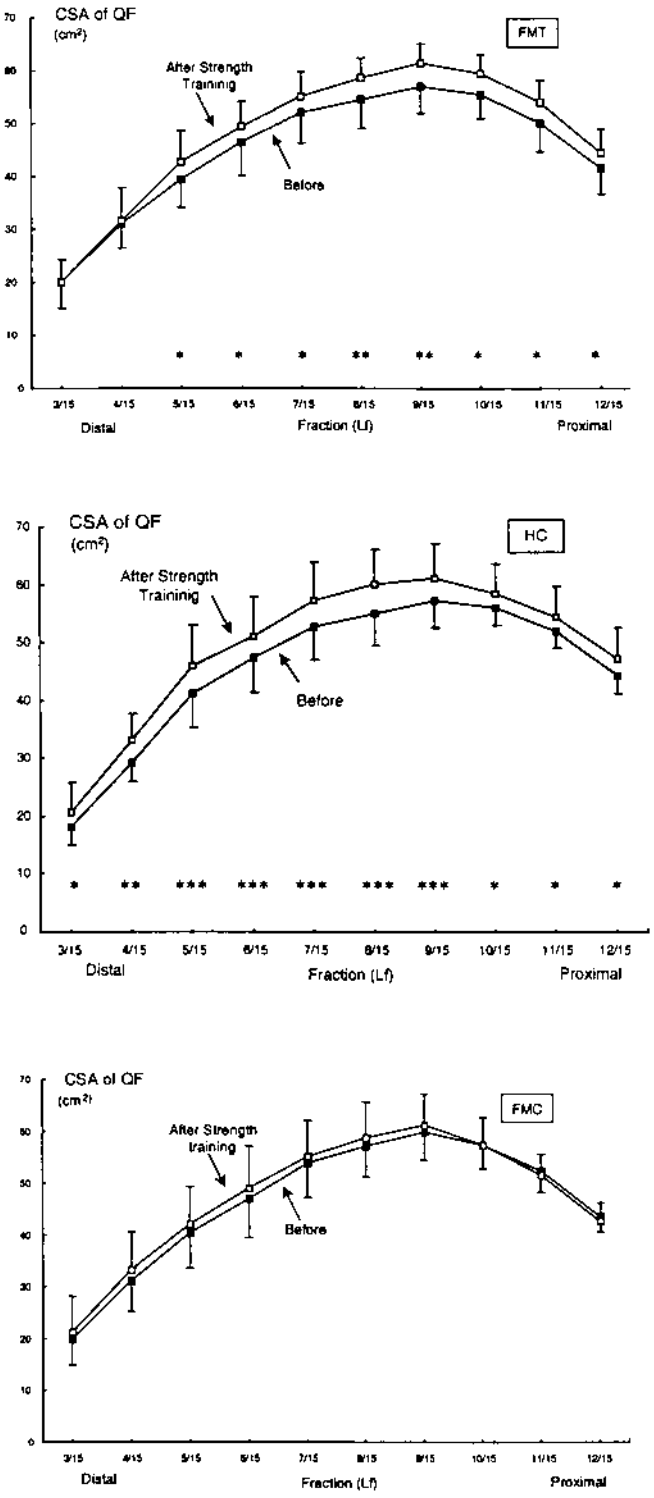

Figure 4. Mean ± SD cross-sectional areas of the total quadriceps femoris (QF) muscle group at the lengths from 3/15 to 12/15 of the femur (Lf) in FMT, HC, and FMC before and after the 21 week strength training period. *p < 0.05, **p < 0.01, ***p < 0.001.

groups by significant increases in the voluntary neural activation of the trained muscles and by significant enlargements in the cross-sectional area of the trained knee extensor muscles. On the other hand, (3) no systematic training induced changes occurred in the basal concentrations of serum total or free testosterone, GH, IGF-I, and DHEAS, but (4) statistically significant acute heavy exercise induced increases in serum GH were observed both before and even more systematically after the 21 week strength training period in both women with FM and healthy women.

The 21 week progressive strength training, although performed only twice a week, led to large gains in maximal strength during the isometric knee extension and flexion actions in both FMT and HC groups. These strength gains in unilateral isometric knee extension actions in the trained FMT were thus closely comparable to strength training induced gains recorded in bilateral isometric and dynamic actions in our FM patients[24]. The data indicate that maximal muscle strength in previously untrained women with FM can readily be increased during progressive strength training independently of the type of testing action, whether bilateral or unilateral and/or isometric or dynamic. Further, twice a week frequency in strength training with progressively increased loading intensity appears appropriate.

Strength training also led to significant increases in the maximal voluntary neural activation of the trained knee extensors. The increased iEMG indicate that the contributing role of the nervous system for strength development was important throughout the training period, and that the force and iEMG increases in our FMT women can be considered normal neuromuscular adaptations to strength training stimuli, as suggested[24]. The magnitude of the coactivation of the antagonist hamstring muscles during the maximal unilateral isometric knee extension was also similar in both groups. However, as expected, the magnitude of the coactivation was minor compared to the coactivation recorded during multi-joint bilateral leg extension actions in both FM patients and healthy women[24]. These data together with our earlier findings[24,26] indicate the presence of a normal neural inhibitory mechanism to protect the musculoskeletal system from injury when the agonist muscles become fully activated. The magnitude of the antagonist coactivation remained rather stable during the experimental training period in both women with FM and healthy controls.

Further, the applied resistance training program also led to significant enlargements in the CSA of the QF in healthy women and in patients with FM. The data showed that the increases in the CSA of the QF took place throughout the length of the femur in both groups. Because the overall magnitudes of enlargement of the CSA of the QF were similar in both groups, the data suggest that skeletal muscles of women with FM retain the capacity to undergo training induced hypertrophy to the same extent as those of matched healthy controls. Taken together, the data strongly suggest that both the magnitude and time course of adaptations of

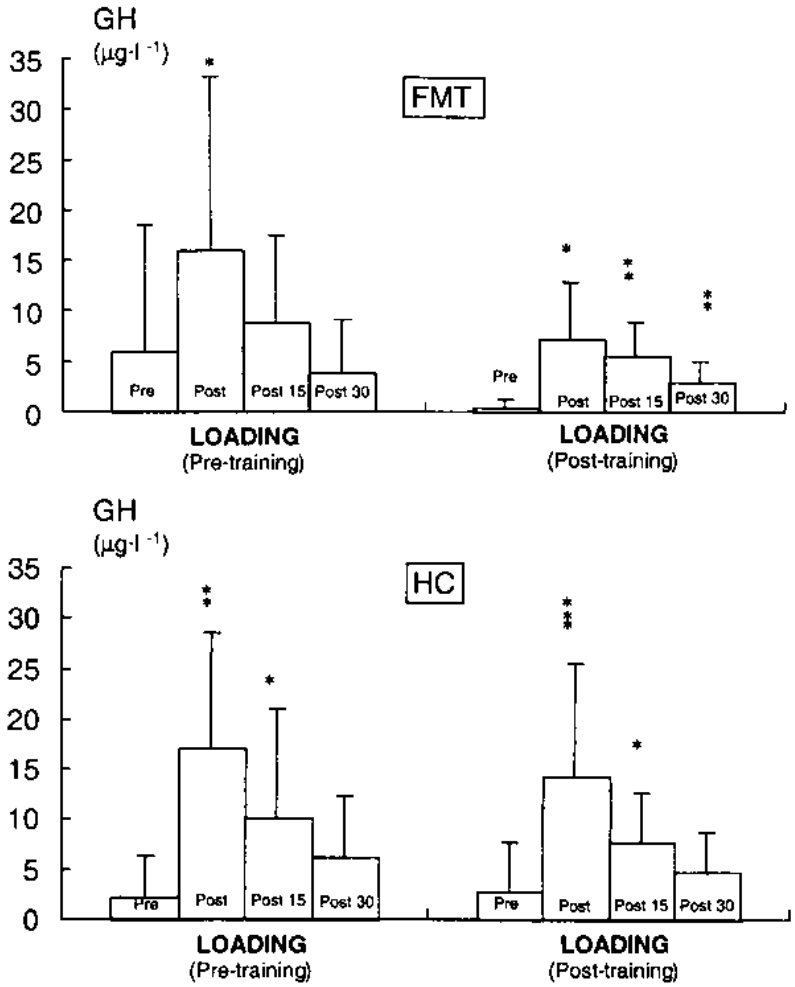

Figure 5. Mean ± SD values for serum GH concentrations before (pre) and immediately after the heavy resistance loading sessions (post), and after 15 min (post 15) and 30 min (post 30) recovery both before (pre-training) and after the 21 week strength training (post-training) in FMT and HC. *p < 0.05, **p < 0.01, ***p < 0.001.

the neuromuscular system to resistance training in women with FM are similar to those taking place in healthy women.

No changes occurred in the number of tender points in the FM groups (Table 1). General pain had a decreasing tendency in the FMT women, but due to great interindividual differences the change was not statistically significant. However, more systematic beneficial effects of strength training could be identified by the clear decrease in fatigue in the strength training group, as in our earlier report[24].

In some studies patients with FM have demonstrated lowered basal levels of GH[12,13] and IGF-I[11]. In this study basal GH concentrations were within normal ranges both in FM and healthy subjects. These results are consistent with those of Jacobsen, *et al*[5], who described comparable basal serum concentrations of GH and IGF-I in premenopausal subjects with FM and healthy women. The data suggest that the FM patients were not characterized by secretory deficiencies of human GH as judged by serum GH and IGF-I concentrations. However, caution must be exercised with this interpretation due to the limited number of subjects, and the fact that this study did not include assessment of nocturnal secretion or the entire 24 h profiles of serum GH and IGF-I.

Lower serum levels of both testosterone and DHEAS in premenopausal women with FM have been reported. Further, low serum androgen levels correlated with poor perceived health status[21]. Although the mean serum levels of DHEAS in our FM patients (both FMT and FMC) were lower than those of HC women, the differences were not statistically significant. However, since the etiology of FM is multifactorial, this does not exclude the possibility that in some individuals hyposecretion of adrenal androgens may be of clinical relevance.

To our knowledge this was the first study to report the acute and longterm hormonal responses of FM women to strength training. We observed no systematic changes during the course of the 21 week strength training period in the concentrations of serum testosterone, free testosterone, DHEAS, GH, or IGF-I in our patients with FM or healthy women. In general, these observations are similar to those in healthy adult men and women when they have utilized typical heavy resistance training programs over a period of a few months[20,29,30].

The data indicate that the overall loading in our training program may have been within normal physiological ranges, because significant muscle hypertrophy did take place and muscle strength increased largely throughout the 21 week training period, with no systematic changes in concentrations of anabolic hormones. The basal levels of anabolic hormones were similar in FM women compared to age matched healthy women, and indicate that the concentrations have been well within the requirements of the typical total body heavy resistance training program applied. The premenopausal FM women seemed to be able to develop their strength and gain muscle mass to about the same extent as healthy women[20] with the low volume total body strength training protocol over the 5–6 month period.

However, in this study only the serum levels of anabolic hormones were measured. It is possible that although, for example, blood testosterone levels would remain unaltered, strength training can induce changes at the receptor level. As with testosterone, no systematic training induced changes were observed in circulating levels of another androgen, DHEAS, in our FMT and HC women during the 21 week period. Further, no systematic changes occurred in GH resting concentrations in either FMT or HC. However, the lack of change in immunoreactive GH may not present the complete picture of the adaptational responses of GH variants to resistance training[20,30]. The lack of change in serum IGF-I may suggests that IGF-I in the circulation may not be a good marker of the implicit activity of the GH–IGF-I system.

Serum total and free testosterone and GH concentrations were measured also during the single heavy resistance session both before and after the 21 week strength training period. It is known that serum testosterone concentrations increase acutely during a typical heavy resistance session in adult men, while the response in women may be minor or even unobservable[18,20,31,32]. Accordingly, no significant acute responses were observed in serum total and free testosterone in either the FMT or HC, either at pre- or post-training.

However, it is known that healthy adult women are able to produce a significant acute exercise induced GH response, although it is minor compared to age matched men[18,20,33]. Thus our data showed that a significant acute increase took place in the mean concentration of GH at pre-training in both HC and FMT, although a somewhat larger interindividual variation in the acute GH response was observed in the FMT than in HC. Nevertheless, the data indicate that the acute exercise induced response in GH in our FMT was already well within normal ranges at pre-training. The data recorded at post-training further showed that the GH concentrations in HC and FMT were elevated immediately after the loading, and remained elevated post-loading up to 15–30 min with less interindividual variation in both groups. Due to the pulsative nature of GH secretion, interpretation of single measures must be cautious. Nevertheless, our observations can be considered an indication of the training induced adaptation of the endocrine system, showing that the acute GH response may become more systematic after strength training in both healthy subjects and women with FM. The magnitude and time duration of the GH response may be important physiological indicators of training induced anabolic adaptations[20].

In summary, the progressive strength training program performed only twice a week but for 21 weeks led to large gains in maximal strength of the knee extensors and flexors in both FM and healthy premenopausal women. The strength gains were accompanied in both groups by significant increases in the maximal voluntary neural activation and by significant enlargements in total CSA of the trained extensor muscles. No systematic changes occurred in basal concentrations of serum anabolic hormones examined during the training period. However, significant acute heavy resistance exercise induced increases of GH did take place in both HC and FMT women before and after the strength training period and at post-training with even less interindividual variation and remained elevated up to 15–30 min post-loading. The data strongly suggest that both the magnitude and time course of adaptations of the neuromuscular system to resistance training in women with FM are completely comparable to those taking place in healthy controls. Second, basal levels of anabolic hormones seem to be similar in women with FM compared to controls, and well within the requirements of the training, when total body (low volume) heavy resistance training programs are utilized. Third, the observations recorded during the acute loading conditions might be considered an indication of the training induced adaptation of the endocrine system, showing that the acute GH response may become somewhat systematic after strength training in women with fibromyalgia and healthy women.

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