J Appl Physiol 105: 1454–1461, 2008.
First published September 11, 2008; doi:10.1152/japplphysiol.90538.2008.

Changes in muscle size and MHC composition in response to resistance exercise with heavy and light loading intensity

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[1]*Institute of Sports Medicine, Bispebjerg Hospital, and Faculty of Health Sciences, Copenhagen University, Copenhagen;* [2]*Medical Research Laboratories, Clinical Institute and Medical Department M (Diabetes and Endocrinology), Aarhus University Hospital, Aarhus; and* [3]*Institute of Sports Sciences and Clinical Biomechanics, University of Southern Denmark, Odense, Denmark*

Submitted 17 April 2008; accepted in final form 8 September 2008

Holm L, Reitelseder S, Pedersen TG, Doessing S, Petersen SG, Flyvbjerg A, Andersen JL, Aagaard P, Kjaer M. Changes in muscle size and MHC composition in response to resistance exercise with heavy and light loading intensity. *J Appl Physiol* 105: 1454–1461, 2008. First published September 11, 2008; doi:10.1152/japplphysiol.90538.2008.—Muscle mass accretion is accomplished by heavy-load resistance training. The effect of light-load resistance exercise has been far more sparsely investigated with regard to potential effect on muscle size and contractile strength. We applied a resistance exercise protocol in which the same individual trained one leg at 70% of one-repetition maximum (1RM) (heavy load, HL) while training the other leg at 15.5% 1RM (light load, LL). Eleven sedentary men (age 25 ± 1 yr) trained for 12 wk at three times/week. Before and after the intervention muscle hypertrophy was determined by magnetic resonance imaging, muscle biopsies were obtained bilaterally from vastus lateralis for determination of myosin heavy chain (MHC) composition, and maximal muscle strength was assessed by 1RM testing and in an isokinetic dynamometer at 60°/s. Quadriceps muscle cross-sectional area increased ($P < 0.05$) 8 ± 1% and 3 ± 1% in HL and LL legs, respectively, with a greater gain in HL than LL ($P < 0.05$). Likewise, 1RM strength increased ($P < 0.001$) in both legs (HL: 36 ± 5%, LL: 19 ± 2%), albeit more so with HL ($P < 0.01$). Isokinetic 60°/s muscle strength improved by 13 ± 5% ($P < 0.05$) in HL but remained unchanged in LL (4 ± 5%, not significant). Finally, MHC IIX protein expression was decreased with HL but not LL, despite identical total workload in HL and LL. Our main finding was that LL resistance training was sufficient to induce a small but significant muscle hypertrophy in healthy young men. However, LL resistance training was inferior to HL training in evoking adaptive changes in muscle size and contractile strength and was insufficient to induce changes in MHC composition.

unilateral training; resistance training; muscle hypertrophy; muscle morphology

PRESCRIPTIONS OF HEAVY RESISTANCE training for muscle restoration purposes have increased over the last decades. Heavy-load resistance training is undoubtedly the most superior way to train when muscle mass and strength improvements are aimed for (13, 15, 21, 39). Heavy resistance training potentially evokes altered muscle architecture [pennation angle (1, 37) and myosin heavy chain (MHC) transitions (47)], selective type II muscle fiber hypertrophy (1), and increased efferent neural drive to the muscle fibers (6), thereby improving muscle quality (i.e., relative change in muscle mass is less than the concomitant gain in muscle strength) (1, 33, 35, 72). However, various patient groups, frail elderly people, and others for whom muscle mass maintenance or improvement is of crucial importance may not tolerate the optimal heavy loading training prescriptions. Sparse knowledge, however, exists on the impact of lighter exercise intensities on muscle mass and function and is further confused by conflicting and inconclusive results (16, 20, 34, 57–59, 61). The significant but diminished effect of medium-load resistance exercise to improve muscle mass is supported by findings after electrical muscle stimulation (12, 55). However, the reported nonsignificant effect of low-intensity training may be due to restricted time and insufficient total loading volume (20, 34, 61), which may possibly also have compromised the detection of similar adaptations after heavier and more frequent training interventions (14, 17). Only a very few previous studies have controlled for differences in total training volume when comparing the physiological effects of light- and heavy-load training regimes (5), and to our best knowledge none has done so when intending to examine the change in muscle mass evoked by these contrasting training intensities. Hence, currently there is a lack of reliable and valid knowledge of the impact of muscle contraction intensity in the lower range of the load continuum on the hypertrophic response. Acknowledging the superiority of heavy loading to improve muscle mass and function, we hypothesized that intense light-load resistance training is sufficient to accrete skeletal muscle mass and that stronger muscles would follow because of that (24, 28, 69). To evaluate the relative potential of the low intensity, a design with the purpose of comparison with a classic heavy loading protocol was made. Except for contraction intensity, training volume is of significant importance when muscle hypertrophy is aimed at (21, 67). Therefore, we carefully controlled training volume.

The aim of the present study therefore was to compare the adaptive changes in muscle size, contractile strength, and MHC composition evoked by resistance training performed at either low or high contraction intensity while equalized for total loading volume. Our working hypothesis was that over a 12-wk intervention period, the duration of a general rehabilitation course, a significant effect on muscle size and function could be detected in response to an intensive, supervised training protocol using low external loading.

METHODS

Healthy, young sedentary men were recruited through newspaper and web advertisements. Twelve men were included in the study after

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examination showed them to be healthy, with no need for daily medication, and sedentary, defined as no organized participation in any sports more than once a week. The subjects were informed about the study protocol, the risks of tests and investigations, and their rights according to the Declaration of Helsinki II, and the protocol was approved by the local Ethical Committee of Copenhagen and Frederiksberg (KF) 01-171/04. One subject was excluded from the study because of low training compliance (not less than a mean of 2.5 training sessions per week was accepted).

Training protocol. Each subject was included in 36 training sessions (12 wk with 3 sessions/wk). The exercise protocol consisted of unilateral resistance training (isolated knee extensions; more details are given below) as outlined in Fig. 1. Briefly, one leg worked against a light load [LL: 15.5% of one repetition maximum (1RM)] while performing 36 repetitions (one repetition every 5th s for 3 min) in each set. The contralateral leg worked against a heavy load (HL: 70% of 1RM), performing eight repetitions (~25 s) in each set. By randomization half of the subjects trained their dominant leg with HL and the contralateral leg with LL, while training was reversed for the other half of the subjects. The exercise consisted of isolated quadriceps muscle contractions performed in a commercial knee extension device (Technogym, Super Executive Line, Gambottola, Italy) with a range of motion of 100° to 30° (0° = full knee extension). The subject remained seated in the training device, alternately working each leg by shifting the predefined loads in the device. A total of 10 sets were conducted during every training session, lasting 35 min in total (see Fig. 1). Notably, similar total contraction work (loads lifted + gravitational internal work) was performed between HL and LL legs in each training session, by progressively applying extra repetitions to the LL leg as the HL leg improved strength faster and to a greater extent than the LL leg. Immediately after each training session subjects consumed a 100-ml nutrient drink (Komplet Näring, Semper, Novartis Healthcare, Copenhagen, Denmark) containing 120 kcal, 5 g protein, 16 g carbohydrate, and 4 g fat plus added minerals and vitamins. Furthermore, subjects were encouraged to eat a larger meal as soon as possible.

Quadriceps muscle cross-sectional area. Magnetic resonance (MR) imaging scans were conducted on a General Electric (GE) MR scanner (Sigma Horizon 1.5 T, GE Healthcare) before and after the training intervention, before any other test measurements were conducted, and after intervention on the third day after the last training session to avoid any effect of fluid disturbances directly related to prior exercise. The protocol was similar to that used previously (29). Briefly, subjects were left relaxed in the supine position for >20 min before the scan was conducted with the legs fixed with Velcro straps. Transaxial images at 10 (distal), 20 (middle), and 30 (proximal) cm above the lateral tibia plateau were obtained. Scans were conducted by professional and skilled radiographers, and the circumference of muscles was manually drawn by skilled personnel blinded in respect to training intensity, reaching an intraobserver coefficient of variation (CV) of 0.6% with the MR scanner software (AGFA web1000).

Muscle biopsy. On a separate day after the MRI scan and after the strength tests were carried out a muscle biopsy was obtained from the lateral part of the vastus lateralis muscle from each leg with a 4-mm Bergström needle (Stille, Stockholm, Sweden) with suction. Briefly, the skin was shaved and disinfected before the local anesthetization with lidocaine 1%. An incision hole was made through which the muscle biopsy was taken. The incision was strapped with SteaStrips and covered with waterproof plaster. The muscle specimen was immediately mounted in Tissue-Tek, frozen in precooled isopentane, and stored at −80°C until further analysis.

Myosin heavy chain analysis. The MHC analysis was performed on the muscle tissue homogenate with sodium dodecyl sulfate-polyacrylamide gel electrophoresis (SDS-PAGE) (8). From each biopsy 50–70 cross sections (20 μm) were cut in a cryostat and placed in vials, and 100–200 μl of lysing buffer pH 6.8 [0.5 M Tris pH 6.8, 10% SDS, glycerol, mercaptoethanol, distilled H_2O, and bromophenol blue (Bio-Rad no. 161-0404)] was added and heated for 3 min at 90°C (22). Between 5 and 20 μl of the myosin-containing samples were loaded on 6% polyacrylamide and 30% glycerol SDS-PAGE gels. Gels were run at 70 V for 42 h at 4°C. Subsequently, the gels were Coomassie blue stained, and MHC isoform content was determined with a densitometry system (Cream 1D, KemEnTec Aps, Copenhagen, Denmark). With SDS-PAGE, three different MHC bands can be separated in adult human skeletal muscle. These bands correspond to MHC isoforms I, IIA, and IIX (38).

Before all testing, subjects were familiarized with the strength tests on a separate day. After a brief warm-up on a Monark cycle ergometer and at submaximal load in the knee extension equipment, subjects were fastened to the seat with straps around the hips and thigh. During 1RM they were allowed to grip the seat with their hands. Subjects were instructed to conduct two unilateral repetitions with the load applied to the lever arm. When a subject was capable of one but not two knee extensions the load was noted, given the 1RM strength. When subjects met for the 10th, 20th, and 30th training sessions they conducted a 1RM strength test as described above.

Maximal dynamic (concentric and eccentric) quadriceps contraction strength was measured with an isokinetic dynamometer (model 500-11, Kinetic Communicator, Chattecx, Chattanooga, TN) at a knee joint angular velocity of 60°/s and range of motion of 90° to 10° (0° = full knee extension) (5, 29). In addition, maximal isometric muscle strength was assessed at 70° knee angle (2, 55). On a separate day before the pretest, the procedures were thoroughly explained and the subjects were familiarized with the dynamometer and the test program. After the training period the tests for isolated quadriceps strength were conducted on the third day after the final training session, just after completion of the MR scan.

After a brief warm-up, the subject was placed in the KinCom dynamometer chair with the hips and thigh strapped to the seat (3, 29). During testing the arms were folded across the chest and strong verbal and visual encouragement was applied by the researcher. After five submaximal attempts separated by sufficient rest periods, the maximal attempts were completed until no increment in peak torque was observed (maximally 6 attempts). Subsequently, isometric strength tests were conducted after 3 min of relaxation. Three maximal attempts were thereafter given by each subject. Online visual feedback of the knee extensor torque produced was provided to the subjects on a PC screen during all testing.

Blood samples. Blood samples for different analyses were drawn at different trials. Therefore, the numbers of subjects enrolled for each analysis differ. However, the conditions were the same irrespective of the trial from which the blood for the different parameters were collected. Subjects arrived at the lab by car in the overnight fasted state. Three days before that meeting, the subjects were instructed to refrain from strenuous exercise or physical work. After 4 h of supine rest, a venous blood sample was collected, after which the exercise protocol was conducted. At 5, 10, 25, 60, and 120 min after cessation blood samples were drawn from the antecubital vein with a polyeth-

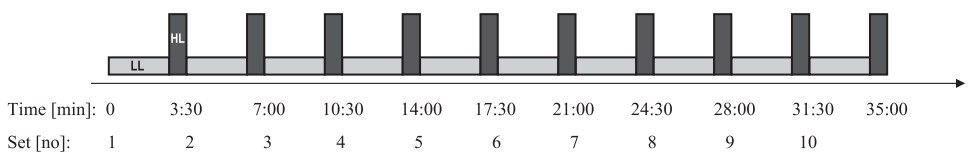

Fig. 1. Exercise protocol design. HL, heavy load [70% one repetition maximum (1RM)]; LL, light load (15.5% 1RM).

ylene catheter. Blood was prepared according to the prescriptions of the respective analyses. All analyses were done as single determinations, and the samples for each parameter from each subject were analyzed in the same analytical sequence.

The following hormone analyses were performed at the Institute of Sports Medicine, Copenhagen: plasma testosterone (testosterone ELISA, DRG Instruments) with an intra-assay CV <5.6%, serum growth hormone (GH) (GH immunoradiometric assay, Biocode-Hycel, Liege, Belgium) with an intra-assay CV <5%, plasma adrenocorticotropic hormone [ACTH; radioimmunoassay (RIA), EDTA-plasma, Nichols Institute Diagnostics, San Clemente, CA] with an intra-assay CV <10%, plasma glucagons (RIA kit, Linco Research, St. Charles, MO) with an intra-assay CV <10%, and serum cortisol (Gammacoat cortisol RIA kit, DiaSorin, Stillwater, MN), intrassay CV <10%. Serum IGF-I, IGF-binding protein (IGFBP)-1, and IGFBP-3 analyses were performed at Aarhus University Hospital. Serum IGF-I was determined by a time-resolved immunofluorometric monoclonal assay (TR-IFMA, Wallac Oy, Turku, Finland) after acid-ethanol extraction as previously described (23) with an intraassay CV <5%. Serum IGFBP-1 was determined by an in-house RIA performed as first described by Westwood et al. (68) and later modified (42), with an intra-assay CV <5%. Serum IGFBP-3 was measured by commercially available immunoradiometric assay (BioSource Europe, Nivelles, Belgium) with an intra-assay CV <5%.

Other measurements. The weighed food registration was conducted before the training intervention was initiated. After thorough verbal instruction, a diary for noting every food item and the amount ingested was given and an electronic balance was offered for borrowing. On three consecutive days subjects were instructed to record their daily intake. Subjects handed in the filled-out diaries, and data were analyzed with Dankost 3000 software (Dansk Catering Center, Herlev, Denmark). Finally, before and after the training intervention subjects were weighed in the morning (wearing only underwear) after an overnight fast.

Statistical analysis. Absolute quadriceps muscle hypertrophy was evaluated by a two-way ANOVA with repeated measures, and the relative changes at each location were compared by paired *t*-tests. 1RM strength and dynamic and static knee extension strength were compared by a two-way ANOVA with repeated measures, and the relative change over the 12-wk period was determined by a paired *t*-test. Blood concentrations of hormones were analyzed by a one-way ANOVA with repeated measures, and the statistical results presented in Table 3 refer to the outcome of the Holm-Sidak post hoc test comparing the postexercise concentrations with the preexercise level. The relative expression of MHC types I, IIA, and IIX in the LL- and HL-trained legs were compared by a two-way ANOVA with repeated measures. When significant changes were found by overall testing, a Holm-Sidak post hoc test was performed to reveal individual differences. Data are presented as means ± SE, and the level of significance was $P < 0.05$. SigmaStat 3.5 (Systat Software, San Jose, CA) was used for statistical calculations.

RESULTS

Eleven male (age 24.7 ± 1.1 yr, height 183 ± 2 cm) weight-stable (pretraining body wt 79.7 ± 4.0 kg, posttraining body wt 79.7 ± 4.0 kg) subjects completed 12 wk of training with a mean training frequency of 2.87 ± 0.04 times per week (no one <2.65 times/wk). They consumed a diet consisting of 18.2 ± 2.5 energy% protein, 55.8 ± 2.4 energy% carbohydrate, and 26.0 ± 2.1 energy% fat.

Quadriceps cross-sectional area. The cross-sectional areas (CSAs) of the quadriceps muscle at the three recording locations (proximal, middle, and distal) are reported in Table 1. The CSAs at all three locations and their average were similar at inclusion in the HL- and LL-training legs. Both legs demonstrated the least hypertrophy at the middle location, with only HL reaching statistical significance ($P < 0.001$). The mean CSA of the quadriceps muscle (Fig. 2) improved significantly in the HL- and LL-trained legs (Fig. 2*A*), although the improvement was significantly larger ($P < 0.05$) in the HL (7.6 ± 1.4%)- compared with the LL (2.6 ± 0.8%)-trained leg (Fig. 2*B*).

Table 1. *Quadriceps cross-sectional area*

	Heavy Load		Light Load	
	Pre	Post	Pre	Post
Proximal	7,302±371	7,852±371	7,384±379	7,619±354
Middle	7,917±296	8,412±320	8,038±305	8,121±309
Distal	3,957±190	4,355±195	4,045±157	4,203±173

Values (in mm^2) are mean ± SE of whole quadriceps muscle cross-sectional area (CSA) at the proximal, middle, and distal locations along the thigh corresponding to 30, 20, and 10 cm above the lateral tibia condyle. Values are the mean of 3 individual measurements from a scan before (Pre) and after (Post) 12 wk of training with either heavy-load [70% 1-repetition maximum (1RM)] or light-load (15.5% 1RM) resistance exercise. A similar and highly significant improvement in CSA was found at the distal and proximal locations after light- and heavy-load resistance training, whereas only in the heavy load-trained leg was the improvement significant at the middle location. Furthermore, at the middle section the CSA was significantly ($P < 0.05$) larger in the heavy load-trained leg than the light load-trained leg after 12 wk of training. No differences in CSA were apparent at inclusion.

One repetition maximum strength. 1RM quadriceps strength before training start and after 10, 20, and 30 exercise sessions is illustrated in Fig. 3*A*. At inclusion the LL-trained leg was slightly stronger than the HL leg. However, after 20 and 30 training sessions the HL-trained leg had improved force production capacity more and demonstrated larger 1RM strength than the LL-trained leg (Fig. 3*A*). However, after both LL and HL training the strength improved significantly within every 10-session training interval. The overall relative improvement was higher during the 30-session period for the HL-trained leg (36 ± 5%) compared with the LL-trained leg (19 ± 2%) ($P < 0.05$, Fig. 3*B*).

Isolated dynamic (isokinetic) and isometric muscle strength. Dynamic quadriceps muscle strength was determined as the peak torque exerted within the range of motion during maximal concentric and eccentric muscle contractions, respectively. Concentric quadriceps contraction strength was equal at inclusion: HL 218 ± 12 N·m vs. LL 224 ± 17 N·m [not significant (NS)]. HL improved concentric strength by 13 ± 5% to 244 ± 14 N·m ($P < 0.05$), whereas LL showed no change (postexercise 229 ± 14 N·m; NS). Before training, maximal eccentric muscle strength was slightly lower in the HL leg (278 ± 15 N·m) than in the LL leg (306 ± 20 N·m) ($P < 0.1$). HL showed increased ($P < 0.01$) eccentric strength (329 ± 22 N·m), corresponding to an increase of 18 ± 4% ($P < 0.01$). In contrast, no changes were observed with LL (postexercise 319 ± 21 N·m; NS). Maximal isometric quadriceps strength was equal at inclusion and increased by 15 ± 4% ($P < 0.01$) from 253 ± 13 to 290 ± 17 N·m ($P < 0.01$) after HL training, while remaining unaltered (6 ± 4%) with LL (277 ± 17 vs. 292 ± 18 N·m; NS).

MHC composition. MHC composition in the vastus lateralis muscle did not differ between HL and LL legs before the start of the study (see Table 3). After training the proportion of MHC IIX isoforms decreased from 7 ± 2% to 3 ± 1% ($P <$

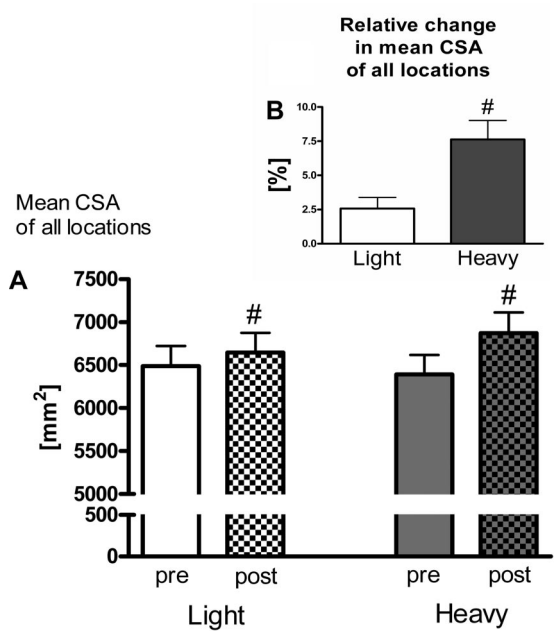

Fig. 2. Quadriceps muscle cross-sectional area (Q-CSA). *A*: absolute Q-CSA as a mean of proximal, middle, and distal measurements (depicted individually in Table 1) before (Pre, open bars) and after (Post, checked bars) 12 wk of training at either light (15.5% 1RM, white bars) or heavy (70% 1RM, gray bars) contraction intensity. No difference was apparent between Q-CSA at inclusion. #$P < 0.05$ compared with corresponding Pre value. *B*: relative change in mean Q-CSA after 12 wk of training at either light (15.5% 1RM) or heavy (70% 1RM) contraction intensity. #$P < 0.05$ difference between the relative changes at the 2 contraction intensities. Data are means ± SE.

0.05) in the HL leg, whereas no change was observed in the LL leg (6 ± 1% vs. 6 ± 1%). No changes appeared for either MHC I or MHC IIA after any of the training intensities.

Blood concentrations. Circulating concentrations of testosterone, GH, IGF-I, IGFBP-1, IGFBP-3, ACTH, glucagon, and cortisol are presented in Table 2. No significant changes in concentration in the early minutes (5–120 min) after a single exercise session compared with preexercise concentration were observed for testosterone, GH, ACTH, glucagon, cortisol, and IGFBP-1 (Table 2). Only IGF-I and IGFBP-3 were elevated at 5 min (10% for each), and IGFBP-3 was elevated at 120 min (7%) as well (Table 2).

DISCUSSION

To our best knowledge the present data are the first to evaluate the adaptive change in muscle size, contractile strength, and MHC isoform expression evoked by resistance training using either low or high contraction intensity, matched for total training volume. The main findings were that in sufficiently nourished, healthy young men training for 12 wk at a nonexhaustive light load intensity (15.5% of 1RM) was sufficient to induce gains in muscle size and 1RM strength. It should be noted, however, that these changes were significantly smaller than those observed after heavy-load (70% of 1RM) resistance training of similar duration and volume. Nevertheless, the results suggest that in situations where heavy-load resistance training is not applicable (e.g., in very early postoperative rehabilitation or in severely ill patients), light-load resistance training may be tolerable and will improve muscle mass and result in concomitant functional benefits.

Training-induced changes in muscle size. Despite major diversities in exercise type and training volume, it can be concluded that when resistance training is conducted at a training intensity heavier than 60% of 1RM muscular hypertrophy is induced along with substantial gains in maximal muscle contraction strength (1, 4, 21, 25, 39, 44, 49, 51, 52, 63, 67, 71). Gains in anatomic muscle CSA of 10–15% have been reported with 10–14 wk of dynamic heavy-resistance training (29, 43, 49). However, some diversity has been shown in the relative improvements along the length of the muscle bulk (45). In the present study we demonstrated a significant mean increase in quadriceps muscle size of 2.6 ± 0.8% (see Fig. 2) after 12 wk of LL resistance training (15.5% 1RM). In comparison, an almost threefold greater gain was observed with HL training (7.6 ± 1.4%, Fig. 2).

The hypertrophic response seen in the HL leg was slightly lower than expected, despite the fact that both total volume and loading intensity (% 1RM) were comparable to previously reported heavy-load training protocols (e.g., Refs. 1, 29). We suggest two possible explanations for this diminished increase. First, a single exercise session did not induce marked changes in the circulating levels of the major anabolic hormones (Table 2). Data support the concept that training involving only a minor fraction of the total muscle mass, as in our protocol, results in a very limited anabolic hormone response (26). Similar hormonal responses are seen after light resistance (48) or endurance (41) exercise. In direct contrast is the response produced when a larger muscle mass is exercised and/or

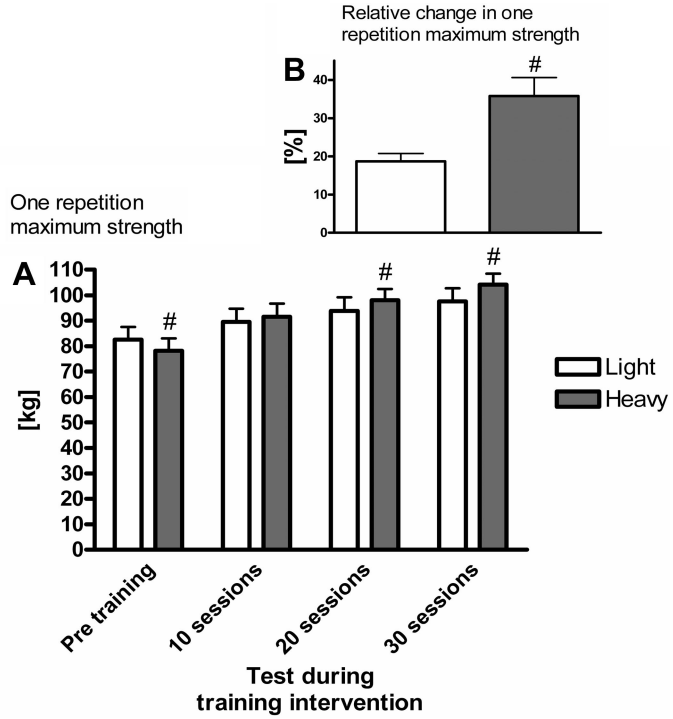

Fig. 3. 1RM quadriceps muscle strength determined in the knee-extensor device. *A*: absolute strength before training start (pretraining) and after 10, 20, and 30 sessions of exercise training. Light, leg trained at 15.5% 1RM; heavy, leg trained at 70% 1RM. #$P < 0.05$ compared with the strength of the Pre value. *B*: relative change in 1RM over the course of 12 wk of resistance training with either light or heavy loads. #$P < 0.05$ difference comparing the relative change following light and heavy load training. Data are means ± SE.

Table 2. *Circulating concentrations*

	Preexercise	Minutes After Exercise				
		5	10	25	60	120
Testosterone, μg/l	4.4±0.4	4.9±1.0	4.8±1.0	4.4±0.9	4.4±0.7	4.5±0.2
GH, mIU/l	2.2±1.4	12.1±5.3	15.3±6.6	21.1±7.9	20.2±12.6	8.4±5.6
IGF-I, μg/l	140±10	154±15*	144±13	144±13	137±13	140±13
IGFBP-1, μg/l	37.0±3.9	33.8±2.9	31.6±3.0	32.2±2.9	30.0±2.4	36.4±3.3
IGFBP-3, μg/l	3,220±80	3,520±90*	3,410±130	3,430±130	3,420±100	3,410±90*
ACTH, ng/l	22.0±2.6	22.6±2.3	21.2±1.6	20.2±2.4	17.6±2.6	23.4±3.3
Glucagon, ng/l	73.2±2.5	70.2±1.8	70.6±5.9	66.5±3.9		63.8±4.3
Cortisol, μg/dl	10.3±1.7	9.9±1.6	9.5±2.3	9.0±1.1	9.0±1.3	9.0±0.7

Values are mean ± SE of circulating levels of testosterone, growth hormone (GH), adrenocorticotropic hormone (ACTH), glucagon, and cortisol ($n = 6$) and of insulin-like growth factor (IGF)-I, IGF-binding protein (IGFBP)-1, and IGFBP-3 ($n = 12$). *Significantly ($P < 0.05$) different from the preexercise concentration revealed by the Holm-Sidak post hoc test. No data exist on glucagon at 60 min after exercise for technical reasons.

more complex training exercises are employed (40). These training modalities would produce a larger relative muscle hypertrophy. Second, the local hypertrophic response in the HL-trained leg was presumably attenuated by the combination of a high training volume (80 repetitions at 70% 1RM) in an unvaried monotonous protocol. Studies using lower volume and different types of exercise (i.e., leg press, knee extension, hack squat) have reported more substantial gains in muscle size (1, 29).

Given that we did not observe any marked systemic endocrine response, the hypertrophy of ~2.5% observed after 12 wk of LL resistance training seems a reliable and valid estimate of the magnitude of muscle size gain that can be expected to occur in response to low-intensity resistance training (21, 34, 57). Furthermore, this finding is important because it demonstrates that a marked and intensity-dependent muscle hypertrophy can be obtained without any systemic anabolic endocrine response. The observed 10% increase in circulating IGF-I and IGFBP-3 presumably originated from a release from the active myocytes, because they are known to increase expression and production of the IGF-axis proteins acutely after exercise (7, 46).

The present data are the first to demonstrate that LL (<20% 1RM) resistance exercise training has the capability to induce muscle hypertrophy (21). These findings are supported by recent data from Drummond et al. (18), who reported that low-intensity exercise induced a myogenic response similar to blood flow-restricted light-load exercise, known to induce muscle hypertrophy. We are aware of only one comparable training study published by Takarada et al. (61), who, however, found no hypertrophy in their control group completing knee extension exercises for 8 wk with light-load intensity (10–20% 1RM) without vascular occlusion. However, their lack of hypertrophy probably was due to markedly reduced training volume and frequency (5 sets of 18 repetitions twice a week for 8 wk) compared with those of the present study (10 sets of 36 reps three times a week for 12 wk). In relation to the recent focus on the effect of vascular occlusion during exercise on the hypertrophy response to even light-load training (60–62), it should be stated that our design allowed the muscle to relax and be oxygenated between contractions.

However, recapping the present data, it turns out that exercise volume seems inversely proportional to exercise intensity when aiming for exercise-induced muscle mass gains. Therefore, several studies have failed to show a muscle-gaining effect of endurance training on skeletal muscle size (16, 30, 56).

Training-induced changes in maximal muscle strength, effects of cross-learning. The primary research question in the present study was to address the importance of exercise muscle contraction intensity for inducing changes in muscle size over time. To reduce the biological variability the within-subject experimental design was chosen. However, we are fully aware of the disadvantages this protocol design creates with regard to the strength measurements (i.e., cross-training). Even though some controversy exists in the findings and interventions leading to cross-training (19), we acknowledge that maximal and submaximal heavy-load unilateral training induces neural adaptations, which involve contralateral cross-training effects (36, 66, 70).

Training strength (1RM) is presumably the strength parameter most influenced by cross-training and neural effects in general, which is shown by the paramount increases already after 10 training sessions. The later improvements, however, were smaller but remained significant after both training intensities. We believe that the continuous 1RM strength improvements caused not only a steady neural adaptation but, specifically for the light-trained leg, a cross-training effect. Part of the improvements we do ascribe to accretion of the contractile apparatus, i.e., muscle size.

Unlike 1RM testing, the slow muscle strength performances conducted in the isokinetic dynamometer tests are assumed not to be affected by cross-learning (50) and hence represent a more reliable estimate of the true training-induced change in maximal contractile capacity. We found that the isometric and slow-speed concentric strength improved as expected with regard to the observed hypertrophy for the HL- as well as

Table 3. *Myosin heavy chain isoform distribution*

	Heavy Load		Light Load	
	Pre	Post	Pre	Post
Type I	63±4	65±4	64±4	60±4
Type IIA	30±3	32±3	31±3	33±3
Type IIX	7±2	3±1*	6±1	6±1

Values are mean ± SE of myosin heavy chain isoform distributions in heavy-load trained (70% 1RM) and light-load trained (15.5% 1RM) vastus lateralis before (Pre) and after (Post) the 12-wk training intervention. *$P <$ 0.05 vs. Pre value.

LL-trained legs. However, for the LL-trained leg, the day-to-day variation and the dependence on noncontrollable confounders for muscle strength measurements with the isokinetic dynamometer assessment method (31, 32) may simply have been larger than the actual strength improvement that would be related to the lean hypertrophy. Therefore, the significant LL training-induced muscle hypertrophy leading to a small increase in functional strength (1RM) was too small to be detected in the dynamometer tests.

Changes in maximal eccentric muscle strength with training interventions have previously been demonstrated to rely strongly on adaptation of neural mechanisms (3, 10). We observed an increased eccentric strength only in the HL-trained leg (see RESULTS), which therefore suggests that HL resistance training affected the neuromuscular function leading to improved strength, whereas LL exercise training did not. Furthermore, no cross-learning effect whatsoever was seen for this adaptive parameter. Also, we did not detect any increase in rate of force development (data not shown), implying that the neural adaptations revealed by any of the training modalities were very limited.

Training-induced changes in MHC protein expression. Heavy resistance training is known to induce a decrease in MHC IIX protein expression (9, 11, 41, 54), which we verified (Table 3) even when applying a protocol using a small muscle group insufficient to exert a systemic endocrine response (Table 2). Furthermore, endurance training is also potent to downregulate MHC IIX protein expression (53) and fiber type IIX presence (41). However, data suggest that the potential of endurance training to decrease MHC IIX protein expression and IIX fiber phenotype is lower compared with heavy resistance training (11, 41, 47). We did not observe any changes in MHC protein expression in the LL-trained leg (Table 3). Because the total performed work was equal between the light and heavy contraction intensities, our data directly demonstrate that contraction intensity rather than performed work is a significant determinant for decreasing MHC IIX protein expression.

The uneven ability of muscle contraction intensities to induce changes in MHC IIX protein expression may potentially have an implication for muscle contractility (11). It has been hypothesized that high abundance of fiber type IIX improves acute and short-lasting muscle contractility (8, 11). However, other adaptations to heavy-load training, where fiber type IIX seems to disappear, favor that regime for the most muscle-strengthening purposes, and the priority of enhancing fiber type IIX may be advisable only after long-term adaptation to heavy resistance training. Thus it is not recommended to refrain from heavy resistance training if the purpose is more powerful and stronger muscles. Therefore, we do not ascribe the differences in MHC protein expression after the two contraction intensities in the present study to exert any functional effect on muscle contractility or to be a motive for choosing any intensity in preference to another.

Conclusions. The within-subject design of the present study, in which unilateral training was performed involving either light-load or heavy-load exercise at equalized total work, insufficient to exert a systemic endocrine response, provides new direct knowledge on the lean effect of contraction intensity on the long-term anabolic response in skeletal muscle. Even in normally functioning, sedentary young men, the quadriceps muscle that is loaded every day adapts to light-load training when targeted directly. These data oppose the common notion that light-load training only leads to adaptation in muscles that are infrequently used and spared for load-bearing functions (65). Therefore, the significance of the present findings is that even very low contraction intensity (~15% 1RM), performed even as isolated resistance training, is sufficient to induce muscle mass accretion in human skeletal muscle. The responses, however, appear to be greatly attenuated relative to those achieved by use of heavy-load (~70% 1RM) resistance exercise regimes. Regardless, the present data demonstrate that low-intensity resistance exercise in the present settings provides a consistent stimulus for muscle hypertrophy, which suggests that this training modality and volume are fundamentally different from other low-intensity types of training, i.e., high-volume endurance training that conversely may induce muscle atrophy (27, 64).

ACKNOWLEDGMENTS

All the volunteer subjects are sincerely thanked. Without their great enthusiasm and eagerness to participate and complete the training as prescribed, these data would never have been generated. We express our gratitude to Joan Hansen, Merete Møller, Kirsten Nyborg, Ann-Christina Ronnié Henriksen, and Ann-Marie Sedstrøm, who helped us in collecting and analyzing data.

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