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The effects of strength training in patients with selected neuromuscular disorders

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ABSTRACT

MCCARTNEY, N., D. MOROZ, S. H. GARNER, and A. J. MCCOMAS. The effects of strength training in patients with selected neuromuscular disorders. *Med. Sci. Sports Exerc.*, Vol. 20, No. 4, pp. 362–368, 1988. Five subjects with spinal muscular atrophy, limb-girdle or facioscapulohumeral muscular dystrophy, were studied. Measurements pre- and post-training included: maximum isometric, dynamic and isokinetic strength, in single-arm curl and double-leg press exercises; contractile properties of the elbow flexors; computerized tomography of the upper arms and thighs; muscle biopsies from the biceps brachii muscle of each arm in three subjects. Dynamic weight training was performed 3 times per week for 9 wk; exercises comprised unilateral arm curls (the contralateral arm acted as a control), and bilateral leg press. Strength increases in the trained arm were between 19 and 34%, and from −14 to +25% in the control arm; leg strength increased from 11 to 50%. Moreover, the pre-training maximum load could be lifted from 3 to 48 times in the trained limbs, and from 1 to 13 times in an untrained limb before fatigue. Contractile properties of the elbow flexors were unchanged with training, but pre-intervention, three subjects demonstrated incomplete motor unit activation. Most of the gains in strength were apparently due to a neural adaptation, rather than muscle hypertrophy. The tomograms and biopsy samples were inadequate to determine muscle, or muscle fiber areas with confidence; they did indicate however, no additional overt muscle structural damage. Strength training may be a potentially useful therapeutic option in the management of selected neuromuscular disorders.

NEUROMUSCULAR DISORDERS, MUSCLE STRENGTH, CONTRACTILE PROPERTIES, FATIGUE, WEIGHTLIFTING TRAINING, MUSCLE ADAPTATIONS

It is well documented that progressive resistance strength training increases muscle size, strength and endurance capacity in healthy individuals (16). In neuromuscular disorders, however, the situation is far from clear; there are anecdotal reports of exercise-induced muscle structural damage and weakness (2, 7) and other claims of modest improvements in strength with no apparent additional morphological damage (21, 22). Few studies have examined the problem systematically using objective measurement techniques, and the majority of investigations have utilised patients with Duchenne muscular dystrophy, including some who had lost more than 50% of their muscle mass (20). It may be expected that such individuals would have only a limited potential for improvement, although gains in strength have been reported (4) in one carefully controlled trial. On the other hand, patients with the limb-girdle or facioscapulohumeral forms of muscular dystrophy, or spinal muscular atrophy, often retain a significant proportion of their muscle mass (9), and thus may harbor a greater potential for improved function (21).

The purpose of the present investigation was to examine the effects of progressive resistance strength training on muscle strength, size, and structure, in patients with limb-girdle or facioscapulohumeral muscular dystrophy or spinal muscular atrophy. A feature of this work has been the recording of the isometric twitch torque in the biceps-brachialis complex. In addition, the interpolated twitch technique described by Belanger and McComas (1) has been used to assess the amount of effort imparted to a voluntary contraction.

METHODS

Five subjects took part in the study; two males and one female with spinal muscular atrophy, one male with limb-girdle muscular dystrophy, and one female with the facioscapulohumeral form. Although spinal muscular atrophy is a degenerative disorder of motoneurones, and the two dystrophies are usually considered myopathies, they share many clinical features. In relation to this study, common to the three conditions is a slow progression of the disease process, and prominent weakness of proximal muscles [for a comprehensive review see McComas (9), pp. 160–165]. Descriptive characteristics of the subjects are listed in Table 1. Clinical assessment of the patients over the past few years indicated that their conditions were slowly progressive, none was deteriorating rapidly. After a detailed description of the procedures involved in the study, including the known risks, the subjects gave their signed informed consent to participate. Approval for the proj-

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TABLE 1. Descriptive details of the subjects

Gender	ID	Diagnosis*	Age of Onset	Age (yr)	Height (cm)	Mass (kg)
F	○	S.M.A.	6	20	157	74
M	●	S.M.A.	38	58	170	75
M	◇	S.M.A.	35	50	170	81
M	□	Limb-girdle M.D.	42	52	168	65
F	▲	F.S.H.	42	60	157	51

* S.M.A., spinal muscular atrophy; M.D., muscular dystrophy; F.S.H., facioscapulohumeral dystrophy.

ect was obtained from the hospital's ethics committee. The qualifications demanded of the patients for entry into this study resulted in a relatively small number being eligible; thus, patients had to be, 1) below 60 yr (to avoid the complication of aging phenomena (3); 2) available for three ½ d for each of 9 wk; 3) easily transported to the University; 4) not severely incapacitated, yet demonstrating weakness in activities of daily living, and on clinical examination; and 5) free of complicating illnesses (especially hypertension and ischemic heart disease).

Prior to, and following the training period, the subjects participated in several tests to investigate muscle structure and function. One female subject was too weak to take part in any of the procedures involving the arms.

Maximal dynamic strength. The voluntary strength of the elbow flexors of each arm was measured during single-arm curl exercises performed on a custom designed pulley device, with the load attached via a cable to a machine handle (Rubicon Industries); the upper arm was stabilized by a curl pedestal. The knee extensors were tested during double-leg press exercise carried out on a Global Gym (4141, SR14) multistation apparatus. The maximum voluntary strength was defined as the load which could be lifted once only, throughout the complete range of movement. After a rest period the testing was repeated to account for any habituation to the apparatus.

Isokinetic strength. The maximal isokinetic strength of the elbow flexors of each arm separately, and the knee extensors of both legs, was determined using an isokinetic dynamometer (Cybex 11, Ronkonkoma, NY) throughout the full range of angular velocities of the instrument. The test of elbow flexor strength was conducted as described previously (15); the subject was seated with the upper arm stabilized on a padded table, and the elbow joint axis was aligned with the axis of the dynamometer lever arm. The subject grasped the handle on the lever arm with the forearm supinated, and performed three maximal concentric contractions, interspersed with 45 s of rest, at each of the chosen angular velocities. The series of contractions were conducted at lever arm angular velocities of 0.52, 2.09, 3.14, 4.19 and 5.24 rad/s (30, 120, 180, 240 and 300°/s), selected in random sequence. Subjects began the contractions with the elbow fully extended, and were instructed to continue exerting maximal effort throughout a full range of movement. The voluntary strength of the knee extensors was measured with a Cybex (Lumex, Ronkonkoma, NY) leg press apparatus, coupled to a Cybex 11 isokinetic dynamometer, described in detail elsewhere (19); testing was carried out at joint angular velocities of 0.26 and 1.31 rad/s (15 and 75°/s) (lever arm angular velocities of 1.05 and 5.24 rad/s), selected in random order. Subjects were seated, and commenced each maximal contraction from an initial knee joint angle of 1.57 rad (90°), progressing through the complete range of movement to full extension. In both procedures, the highest torque generated in three trials was considered the peak torque.

The torque signals from the instruments were recorded on a two channel oscillograph recorder (Hewlett Packard 7402A, San Diego, CA), and analyzed for impact torque and peak torque. Impact torque may be defined as an initial torque overshoot, resulting from the accelerating limb and dynamometer lever arm first engaging the resistance offered by the dynamometer; peak torque is the highest torque produced after the impact torque [for a detailed discussion of impact torque vs peak torque, see Sale et al. (15)].

Muscle contractile properties. The isometric evoked, and voluntary strength of the elbow flexors was measured on a custom-made arm stabilizing apparatus; the evoked responses were used in the measurement of muscle contractile properties—peak twitch torque, time to peak torque, and half relaxation time. The apparatus comprised two aluminum plates, one fixed in the horizontal plane on which the upper arm rested, the other which could either be fixed or freed to rotate about a shaft. The subject's forearm was placed on the second plate in the supinated position and held by Velcro straps; the elbow joint was aligned with the shaft to ensure that changes in the position of the rotating plate and forearm were coincident. At any chosen joint angle the rotating plate could be clamped to the shaft to prevent further movement, and to facilitate isometric contractions. The torque generated during contractions was detected by a foil strain gauge mounted on the shaft, and transmitted to a storage oscilloscope (Hewlett Packard 120 1B) and computer (PDP 11-03, Digital Equipment) for on-line analysis.

Twitch contractions were evoked by percutaneous electrical stimulation via two large lead plate electrodes, which were wrapped in moistened gauze impregnated with conducting medium. One electrode was located over the belly of the biceps and the other was placed on the palmar surface of the forearm just below the elbow. Stimuli were rectangular voltage pulses of 50- or 100-μs duration, produced by a Devices stimulator (Medical Systems Corp.). A maximal twitch contraction was considered to have been evoked when no further increases in torque could be produced by further increases in the stimulus intensity.

The evoked and voluntary contraction torques were measured in the elbow flexors of each arm at joint angles of 1.31, 2.09, and 2.88 rad. The sequence of angles for testing was randomized, and there were two trials interspersed with 45-s rest periods; the highest value in the two trials was taken as the peak torque. To obviate the likelihood of twitch potentiation by prior voluntary contractions, the evoked responses were recorded at all three joint angles before the measurement of voluntary strength. The completeness of motor unit activation during the maximal voluntary contractions was assessed by the interpolated twitch technique, described in detail elsewhere (1). Briefly, if the application of a maximal indirect stimulus during a short maximum voluntary contraction fails to evoke any additional torque, it is considered that all motor units are recruited and firing at optimal frequencies for tension development.

Computerized tomography. Computerized tomographic scans of the upper arms and both thighs were obtained as described previously (8); it was intended that the tomograms be used to assess the severity of muscle degeneration, and for the measurement of muscle cross-sectional areas.

Muscle fiber characteristics. The three male subjects (Table 1) consented to needle biopsy of the biceps muscle of each arm for the determination of muscle fiber characteristics. Target measurements included fiber type distribution, mean fiber area and total fiber number, as described previously (8).

Training regimen. Dynamic strength training was performed on three occasions each week for nine weeks. Subjects trained the elbow flexors of one arm only, selected at random, on a custom designed arm curl apparatus; the contralateral arm served as a within-subject control. The knee extensors were subjected to bilateral leg press exercise on a Global Gym (4141-162) multistation training device. Subjects initially performed 2 sets, and progressed to 4 sets of 10 and 12 repetitions, in arm and leg exercises respectively. The resistance schedule was as outlined below.

Weeks	
1 and 2	2 sets at 40% of the maximum voluntary contraction (MVC).
3	2 sets at 50% MVC.
4	3 sets at 50% MVC.
5	1 set at 50% and 2 sets at 60% MVC.
6 and 7	1 set at 50% and 3 sets at 60% MVC.
8	1 set at 50%, 2 sets at 60% and 1 set at 70% MVC.
9	1 set at 50%, 1 set at 60% and 2 sets at 70% MVC.

RESULTS

Dynamic arm strength. Prior to training the maximal dynamic arm curl strength ranged from 19 to 127 N (1.9–13 kg) in the arm to be trained, and from 18 to 118 N (1.8–12.0 kg) in the control arm. Both arms improved in strength following the intervention period, but the mean increase in the trained arm (34%) was more than double the mean gain in the control arm (16.4%). There was considerable inter-subject variability in the improvement that was noted (Fig. 1), but only one individual increased strength more in the control arm than in the trained limb. Following the intervention period the subjects were able to lift their pre-training maximum load with the trained arm an average of 21 (range 3–48) times before fatigue (Fig. 1), and an average of 8 (range 1–12) times in the control arm.

Isokinetic arm torque. Prior to training the impact torque generated by the elbow flexors at the five angular velocities was similar in each arm (Fig. 2), but following the conditioning period the trained arm showed a greater improvement at the three highest angular velocities (Fig. 2). When the data were corrected for the impact component however, the torque produced by the trained arm was only slightly greater than in the control arm (Fig. 2); the mean improvement over the five angular velocities following training was 32% in the trained arm compared to 25% in the control arm. Once again there were considerable differences in the magnitude of improvement between subjects (Fig. 3).

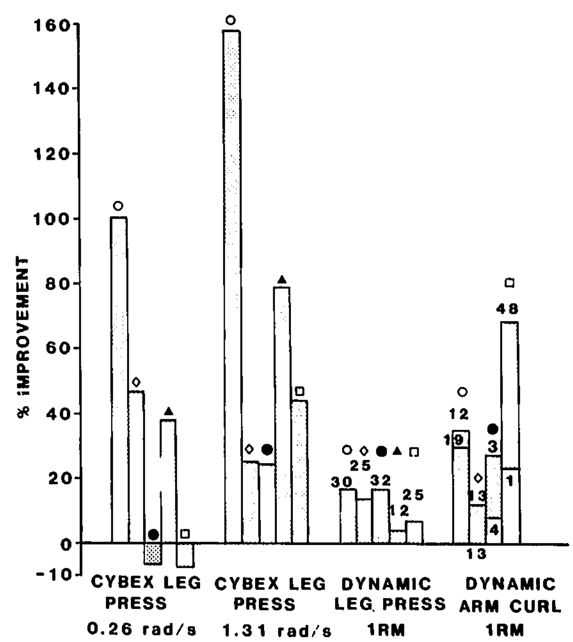

Figure 1—The individual relative improvements in isokinetic and dynamic strength following the training regime in the trained (*gray bars*) and untrained (*white bars*) limbs. The numbers associated with the dynamic results denote the number of times post-training that the pre-training maximum load could be lifted before fatigue. The symbols ○, ●, ◇, □, and △ identify the patients as listed in Table 1.

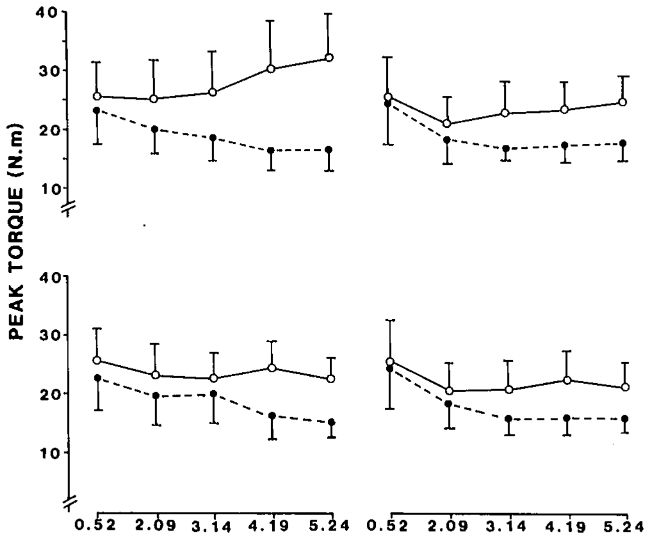

Figure 2—The peak torque generated in isokinetic elbow curl exercise on the Cybex apparatus at 5 angular velocities before (●---●), and after ○——○) training, in the trained (*left panel*) and untrained (*right panel*) arm. The upper part of the figure displays the impact torque; the lower half is the peak torque, adjusted for the impact component (see text). The data are presented as the mean ± the SEM, for the sake of clarity.

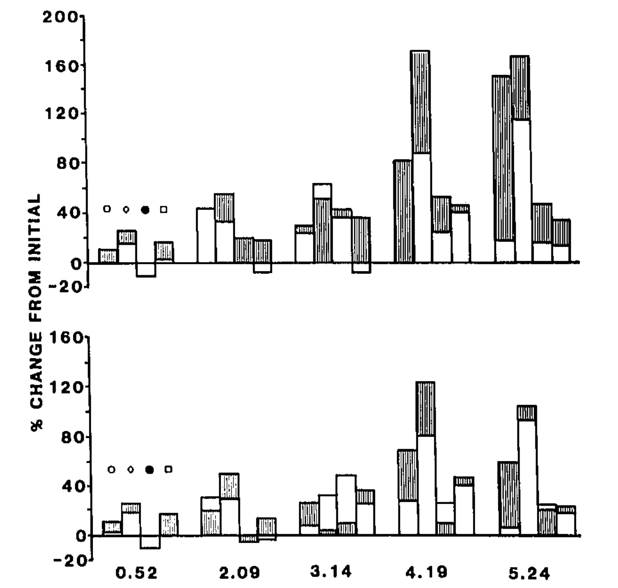

Figure 3—The individual relative improvements in isokinetic arm strength following the training regime, in the trained (*striped bars*) and untrained arm (*white bars*). The upper figure displays the change in the impact torque; the lower half is the peak torque, adjusted for the impact component. At each velocity the individual patient data are depicted according to the symbols listed above the results at 0.52 rad/s, and in Table 1.

Voluntary and evoked muscle strength, and contractile properties. Prior to training, the maximum voluntary isometric torque that was produced at the three joint angles tested ranged from 4.6 to 60.9 N·m in the control limb (mean values of 32, 30 and 20 N·m, at angles of 1.31, 2.09 and 2.88 rad respectively), and from 4.9 to 52.9 N·m in the arm to be trained (mean values of 28, 27, and 17 N·m at 1.31, 2.09, and 2.88 rad). Following the intervention period the performance in the trained arm improved by an overall mean value of 19.1%, whereas the control arm experienced a decline in maximal voluntary torque of 14.1%.

The interpolated twitch technique was employed at a joint angle of 2.09 rad, and the results indicated that prior to training, three of the four subjects were unable to fully activate the elbow flexors in either arm (62–98% activation in the trained arm versus 48—77% in the control arm); following the intervention period all subjects were able to achieve complete activation in both arms.

The evoked twitch properties of peak torque, time to peak torque and half relaxation time, did not demonstrate any systematic changes over the course of the study; a composite of the measures obtained at the three elbow joint angles tested is portrayed in Figure 4.

Dynamic leg strength. At the start of the study, the maximal load that could be lifted by the subjects in a bilateral leg press manoeuvre ranged from 343 to 1765 N (35–180 kg), and there was a mean improvement of 11% following the training (Fig. 1). Although the pretraining maximum load was an average of 90% of the

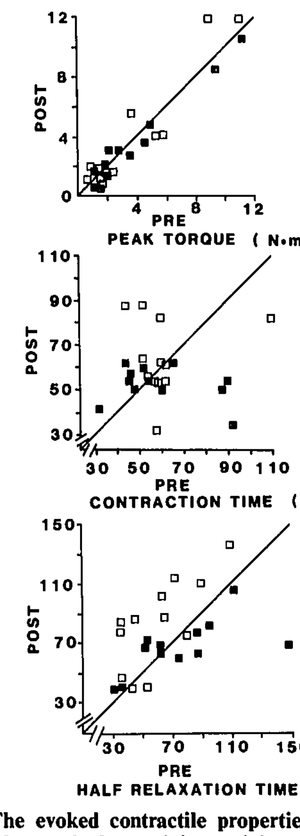

Figure 4—The evoked contractile properties of the elbow flexors measured before and after training at joint angles of 1.31, 2.09 and 2.88 rad: (■) trained arm; (□) untrained arm.

post-training maximum, at the end of the study it could be lifted by the subjects from 12 to 32 times before exhaustion (Fig. 1).

Isokinetic leg torque. Prior to training the maximal torque generated in a bilateral leg press movement at the two angular velocities ranged from 76 to 620 N·m. Following the intervention there was a mean improvement of 34% and 66% at the angular velocities of 0.26 and 1.31 rad/s, respectively, but there was a large intersubject variation in the response (Fig. 1).

Computerized tomography. The computerized tomograms revealed varying degrees of muscle tissue ablation, and replacement by fat and connective tissue. For this reason it was concluded that an overall measure of muscle cross-sectional area was of limited value in these patients, and the tomograms were analysed subjectively. As far as could be determined subjectively, the tomograms revealed that the strength training did not result in any additional areas of obvious damage within the muscle.

Muscle biopsies. The biopsy samples from the three subjects who consented to the procedure indicated diffuse muscle fiber wasting, and replacement by fat and connective tissue. The healthy residual fibers varied markedly in size and shape, but on average the cross-sectional areas were within normal limits for sedentary healthy individuals (8). Although it was intended to compare the cross-sectional areas of the various fiber types before and after training, the biopsy samples did not yield a sufficient number of fibers to allow for an accurate assessment (8). The one observation that could be made was that the training did not appear to induce any further overt structural damage.

DISCUSSION

The purpose of the present study was to investigate the effects of progressive resistance dynamic strength training on muscle strength, size and structure, in patients with slowly progressive neuromuscular disorders.

It was intended that the maximum cross-sectional areas of the elbow flexors and knee extensor muscles would be measured before and after training by computerized axial tomography, to quantify any changes that may have occurred. Unfortunately, the tomograms generally revealed diffuse replacement of muscle fibers by fat, which rendered a measure of total cross-sectional area rather meaningless. Nevertheless, information obtained by tomography on the extent of muscle ablation may be very useful in future similar studies, to help set realistic targets for improvement. For example, in the present study the individual with the strongest elbow flexors in all modes of testing also demonstrated the best preservation of the flexor muscle mass. The tomogram from this subject is contrasted in Figure 5 with that from another patient which reveals severe infiltration of the muscle by fat and connective tissue; this subject was too weak to take part in any of the testing or training of the arms. It appears that computerized tomography is a valuable technique for diagnostic purposes and for following the course of muscle degeneration (6) in patients with muscle diseases, but probably cannot be used in all cases to obtain reliable estimates of muscle cross-sectional area.

As with the computed tomography the muscle biopsy samples from the three subjects who consented to the procedure were inadequate for quantitative purposes due to the limited numbers of healthy fibers contained within the specimens; the average cross-sectional areas of the apparently healthy residual fibers were within the normal range of 3000—5000 μm^2. Examination of the biopsy specimens did indicate, however, that the strength training had not induced any obvious additional gross muscle structural damage, contrary to the conclusions inferred from some previous reports (2, 7).

The major finding in the present study was that the

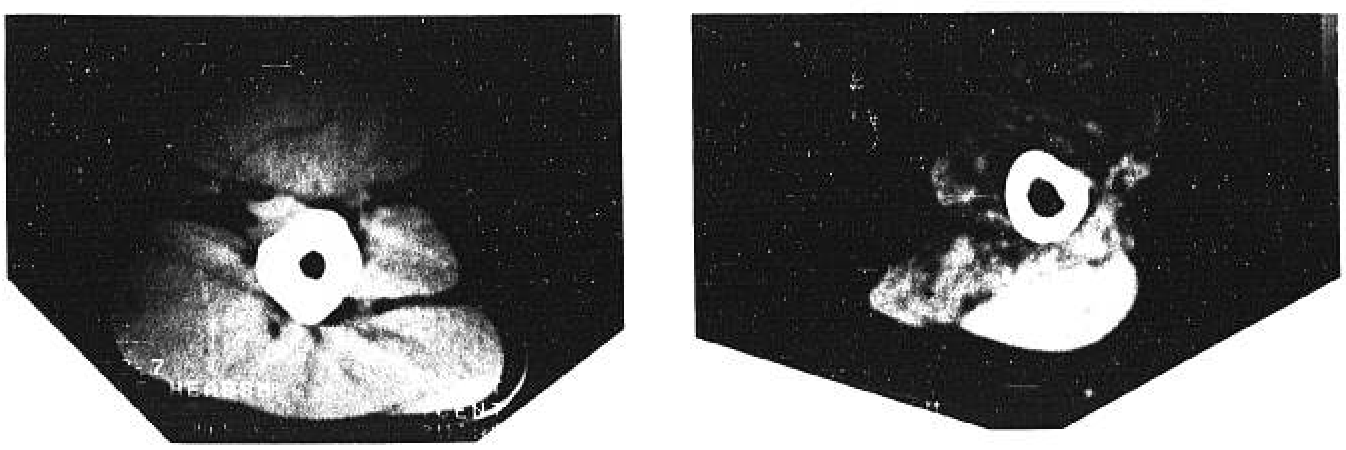

Figure 5—Computerized tomograms of the upper arm in the two subjects with the strongest (*left panel*) and weakest (*right panel*) elbow flexors. The scans demonstrate good preservation of the elbow flexors in the strong subject, and significant replacement of muscle by fat and connective tissue in the weak patient.

subjects demonstrated considerable gains in strength as a result of weightlifting training (Fig. 1). In addition to gains in strength, the training produced substantial improvements in endurance capacity. At the end of the study the subjects were able to lift their pretraining maximum load from 3 to 48 times in the trained limbs, and from 1 to 12 times in an untrained limb, before fatigue (Fig. 1). In a patient population in which the dominant symptom is premature weakness and fatigue (10), such notable gains in maximum strength and endurance may assume major importance, and allow the individual to carry out tasks of daily living such as climbing stairs and lifting objects, with greater ease. In this regard the increases in endurance capacity may be more meaningful, especially when one considers that the pre-training maximum load that could be lifted repeatedly following the exercise intervention was on average 84% (90% with the legs, 77% with the arms) of the post-training maximum load. Thus, the gains in endurance were at a high percentage of the muscles' improved absolute strength capabilities.

This finding of enhanced endurance may have significant application to the clinical assessment of functional capacity in neuromuscular disorders. The most common method to estimate residual function in this patient population is to subjectively gauge the maximum strength by manual muscle testing. In addition to the imprecise nature of such procedures, they yield no information on functional fatigue resistance, when muscles are required to contract repeatedly at submaximal intensities (due to these limitations manual muscle testing was not utilized in the present investigation). We have reported previously (10) that some patients with extraordinarily weak muscles may exhibit much greater than normal fatigue resistance, particularly when there is selective atrophy of Type II fibers. Based on these results it would seem prudent to conclude that isolated measures of strength may not accurately reflect a patient's capacity to function in many activities of daily living, neither do they necessarily provide evidence of improvement following any therapeutic intervention. An additional, objective assessment of submaximal fatigue resistance may contribute to an improved clinical evaluation.

Improvements in strength with overload training have been attributed to both neural and muscular adaptations (12). Substantial gains in strength occur in the initial few weeks of a training regimen, when there is little demonstrable hypertrophy of muscle fibers (5, 13, 17, 18) thus suggesting a neural mechanism for improvement. Moreover, in studies which have trained one limb, there have been increases in strength in the contralateral limb without any changes in muscle size, muscle fiber size or evoked contraction strength [for review, see Sale (14)]. In patients with myotonic or limb-girdle muscular dystrophy there may be improvements in voluntary strength during one testing session, due to an initial inability to fully activate motoneurones (1).

The results of the present investigation may also be explained in large part by the neural hypothesis. 1) Although the trained arm increased in dynamic and isokinetic strength by an average of 33%, there was a 20% improvement in the strength of the contralateral control limb (Figs. 1 and 3). 2) At the start of the study the interpolated twitch technique confirmed that three of the four subjects were unable to fully activate the elbow flexors in either arm, but after the training period all of the patients could achieve complete activation. 3) There was a substantial increase post-training, in the ballistic torque to peak torque ratio recorded during Cybex testing of the arms at the three highest speeds (Fig. 2), indicating an enhanced ability to overcome the inertia of the dynamometer's lever arm and to accelerate it rapidly (14). 4) The evoked contraction strength of the elbow flexors was unchanged after training (Fig. 4), consistent with minimal muscle fiber hypertrophy (11). These results prompt the conclusion that a major reason for the enhanced strength following training was a neural adaptation. As indicated by the interpolated twitch technique, part of that adaptation was apparently due to the descending motor pathways becoming more efficient in exciting lumbo sacral motoneurones; other possible mechanisms cannot be identified using the present data.

This study has demonstrated that strength training may result in substantial increases in the strength and endurance capabilities of individuals with slowly progressive neuromuscular disorders, without any attendant overt evidence of muscle fiber damage. Further investigations are needed to determine if these increases promote enhanced function in activities of daily living. In the meantime, it would seem prudent for health care practitioners to adopt carefully controlled strength training as a potentially valuable therapeutic approach in the management of selected neuromuscular disorders.

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