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The Positive Effects of Negative Work: Increased Muscle Strength and Decreased Fall Risk in a Frail Elderly Population

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Background. The objective of this study was to determine if a chronic eccentric training intervention, i.e., negative work, could limit or even reverse sarcopenia and its related impairments and functional limitations. Is high-force eccentric training tolerable by elderly people and will it result in improved muscle size, strength, balance, and fall risk?

Methods. 21 frail elderly subjects (mean age, 80 years) experienced 11 weeks of lower extremity resistance training. The experimental eccentric (ECC) group ($n = 11$) performed negative work while exercising on a high-force eccentric ergometer. The active "controls" performed traditional (TRAD) ($n = 10$) lower extremity resistance exercises (weight training). Muscle fiber cross-sectional area and strength, balance, stair descending abilities, and fall risk were assessed prior to and following this intervention.

Results. All ECC subjects who started the negative work intervention completed the study and reported the training to be relatively effortless; they experienced minimal and transient muscle soreness. Both groups experienced a significant increase in muscle fiber cross-sectional area (ECC = 60%, TRAD = 41%). Only the ECC group experienced significant improvements in strength (60%), balance (7%), and stair descent (21%) abilities. The timed up and go task improved in both groups, but only the ECC group went from a high to a low fall risk.

Conclusions. These data demonstrate that lower extremity resistance exercise can improve muscle structure and function in those with limited exercise tolerance. The greater strength increase following negative work training resulted in improved balance, stair descent, and fall risk only in the ECC group. Because low energy cost is coupled to high force production with eccentric exercise, this intervention may be useful for a number of patients that are otherwise unable to achieve high muscle forces with traditional resistance exercise.

A positive feedback of inactivity coupled with muscle wasting and weakness often puts elderly persons at high risk for serious life-threatening falls, the most common cause of injury-related death in persons over 75 years of age (1). Falls, especially while negotiating stairs, result from numerous causes (2,3); however, they are often directly attributed to impairments (in size and strength) in the lower extremity musculature (4–6). Since a large proportion of the highest fall-risk elders are exercise intolerant, an easily tolerated resistance intervention that produces moderate-to-high muscle forces may increase their muscle mass, strength, balance, and stair-negotiating abilities, while also lowering their risk of falling.

Force production in skeletal muscle is highest during negative muscle work (an eccentric contraction) when an activated (contracting) muscle is lengthened by an external load (7–10). Because high-force production is the stimulus for increasing muscle size and strength, the elevated forces produced during eccentric contractions (negative work) could be the most powerful stimulus to promote muscle growth and strength (11–14). A further benefit of eccentric contractions is that the energy required (i.e., oxygen consumed) to produce negative work is trivial relative to the equivalent magnitude (i.e., same force production) of positive work, i.e., when a muscle shortens, displacing an external load (15–17). This low energy requirement results in a perception of much "less effort" to those participating in this exercise. Therefore, the "high force, low cost" abilities of eccentric contractions are thought to be ideally suited to elderly subjects engaging in resistance exercise (14,18,19). Negative work may even be possible for those characterized as exercise intolerant (e.g., patients with moderate-to-severe cardiopulmonary impairments) and at risk for falling. To date, however, chronic high muscle force negative work has not been assessed in this, or any, patient population. This reluctance may be due to the association of eccentric contractions with muscle injury, as any injury in a high-risk patient population could have dire consequences. However, in previous studies with young, healthy subjects, where the exercise is increased gradually and progressively, the muscles: (a) adapt to high eccentric forces of negative work without a muscle injury response (19–22), (b) increase in size (12,19), and (c) strength (8,11,12,19,22,23).

Because negative work requires muscles to contract eccentrically with little demand for energy, yet can overload muscle to a great extent, it may be perfectly suited to elderly exercise-intolerant individuals at risk for falling. This intervention also may be especially appropriate for those

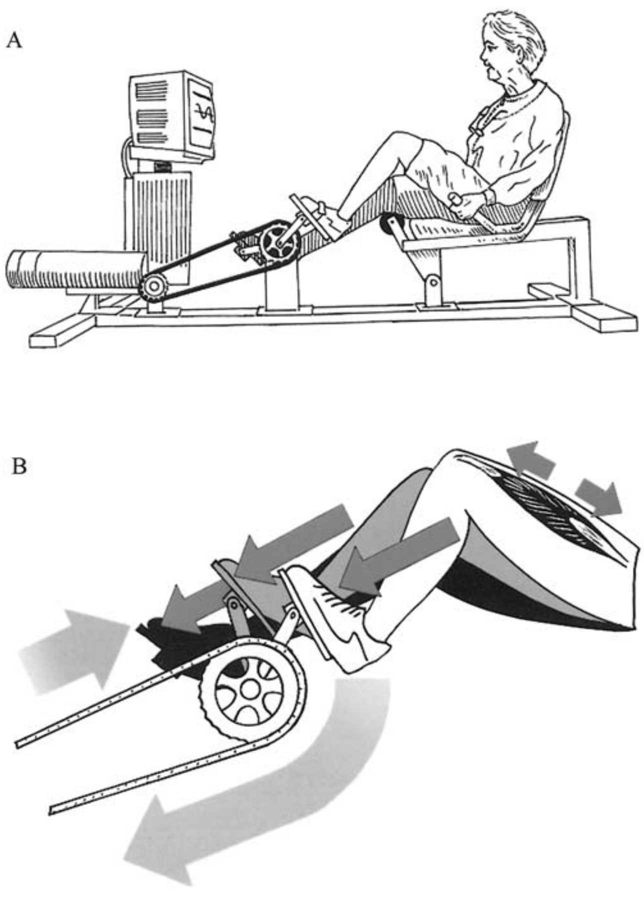

Figure 1. **A**, Negative work resistance exercise was performed on an eccentric ergometer powered by a 3-hp motor that drives the pedals in a backward rotation. The subjects varied their resistance to the reverse moving pedals to match a "target" on a computer monitor. The target was increased very gradually over the first 3 weeks to avoid muscle soreness, but by greater increments subsequently to keep the perceived exercise intensity in a range of "somewhat hard." **B**, As the motor rotates the pedals at a set speed in a reverse direction (large rotating arrows), the subject attempts to slow down the reverse moving pedals (small arrows at foot). Negative work resistance training results because the magnitude of force produced by the motor exceeds that produced by the subjects, thus the pedals continue backward, resulting in the eccentric lengthening of the quadriceps muscles (small arrows at thigh).

elderly persons with a diminished ability to safely descend stairs (hence the high incidence of falling while descending stairs), due in part to impaired submaximal eccentric muscle abilities (24–27). Therefore, the purpose of this brief article is to describe the structural and functional impacts of a high eccentric muscle force, negative work resistance training intervention on a high fall-risk elderly population.

METHODS

Subjects

Twenty-one adult patients (mean age, 80.2 years; age range, 70–93; 11 male, 10 female) who had been participating in an outpatient cardiopulmonary rehabilitation program (phases II–IV) at a university medical center consented to 11 weeks of lower extremity resistance exercise training. The group of interest ($n = 11$) exercised on a recumbent, high-force eccentric, leg cycle ergometer (ECC group). The comparative group ($n = 10$) used a traditional resistance exercise program of weight machines and free weights (TRAD group) for their lower extremity resistance exercise, served as "active controls." Both groups exercised 3 times per week and devoted 10–20 minutes to lower extremity resistance exercise. All subjects suffered from sarcopenia (age-related loss of muscle mass) so that their individual performance measures classified them as having balance impairments and poor stair descent abilities, and they were at a "high risk" for falling, as measured primarily by the timed up and go test (greater than 14 seconds) and secondarily by the Berg balance scale and their stair descent time (28,29). In addition, their history of cardiovascular (e.g., chronic heart failure, myocardial infarction, coronary artery bypass surgery, heart valve replacement, pacemaker) and peripheral vascular (e.g., peripheral vascular disease, hypertension, diabetes mellitus) impairments prohibited strenuous exercise even for brief periods.

Eccentric Negative Work Resistance Exercise and Perceived Exertion

The ECC group performed negative work resistance exercise of the lower extremities with a custom-made eccentric cycle ergometer [described previously (19,22)] powered by a 3-hp motor that drives the pedals in a backward rotation while the subject attempts to slow down (by resisting) the reverse moving pedals (Figure 1). Training intensity was determined by the subject's perception of exertion, using a Borg rating of perceived exertion scale (30), the familiar scale used to gauge all exercises in the cardiopulmonary rehabilitation program. To ensure a gradual and progressive acclimation to the negative work exercise, each ECC subject started at the lowest exertion level on the Borg scale, "very, very light." By the third week (9 training sessions) the perceived exertion had gradually increased through the "very light" and "fairly light" levels, eventually reaching an exertion level of "somewhat hard." The "somewhat hard" exertion effort is a typical goal for many cardiopulmonary patients in the facility where this study was performed. The Borg perceived exertion scale provided a regular and reproducible progression among all the ECC subjects (see Figure 2).

Traditional Weight Training Resistance Exercise

The TRAD group used free weights and weight machines for their lower extremity resistance exercises. The TRAD group progressed their lower extremity resistance exercises (e.g., leg press, leg extension, mini-squat) by increasing their resistance, i.e., when 10–15 repetitions were considered "easy" to perform, the weight was increased to a level where 6–10 repetitions were "difficult."

Muscle Soreness

Muscle soreness was assessed before every training session, only with the ECC group, on a 15-cm visual analog scale anchored at one end of the scale (0 cm) by the descriptor "no soreness" and at the other end (15 cm) by "worst possible soreness." The numerical muscle soreness result was determined by measuring (in cm) where the subject noted and marked their leg soreness to be along the 15-cm scale.

Knee Extension Isometric Strength

Knee extension isometric strength of both the ECC and TRAD groups, measured as N of isometric force (at 45° of knee flexion), was measured weekly as well as before and following the 11-week training session with a dynamometer (Microfet, Hoggan Health Industries, Inc., Murray, UT) secured to an immovable frame. In all instances, the average of 3 repetitions (2-minute rest between repetitions) was recorded. Because we have previously documented a "learning effect" (i.e., upwards of >50% of the effect possibly being secondary to learning) (19) when measuring strength weekly, we believe the initial apparent improvement in strength in this elderly population may be due to learning the task. For that reason, to document strength gains, we used the isometric strength recorded at week 3 and compared that with the strength measurements following 11 weeks of training; this resulted in a conservative "control" for any possible learning effect.

Quadriceps (Vastus Lateralis) Muscle Fiber Cross-Sectional Area

Both before and after the 11 weeks of training, a percutaneous muscle biopsy of the vastus lateralis was harvested on those subjects (ECC $n = 4$, TRAD $n = 3$) for whom a biopsy was not contraindicated (e.g., those on blood-thinning agents), then immediately frozen in isopentane, cooled in liquid nitrogen, and processed for fiber area measurements. To calculate muscle fiber cross-sectional area, a 10-μm thick frozen cross-section from each muscle biopsy was incubated with a primary antibody for the membrane protein laminin (Sigma, Perth, Australia), which defines each muscle fiber boundary as described previously (19). A Zeiss microscope interfaced to a video imaging system (Scion Corporation, Frederick, MD) was used to store a digital image for analysis. The cross-sectional area of each fiber (determined from approximately 100 fibers per biopsy sample) was determined at an objective magnification of 10× and all of the pixels enclosed within the outlined boundary were calculated.

Balance, Stair Descent, and Fall-Risk Performance

A battery of performance tests, regularly employed with elderly populations (28,29), assessed balance (Berg balance scale), the ability to descend stairs safely (timed-stair descent), and fall risk (timed up and go) before and after training. The Berg balance scale provides a validated assessment of overall balance in elderly subjects. The Berg balance scale tests balance functions that a rater scores on an ordinal scale for each task. The 14 tasks can be scored up to 56 points, the higher the score the better the balance abilities. The timed stair descent is an excellent measure of eccentric muscle function capabilities and is the time (seconds) it takes to safely descend 2 sets of 12 stairs (a commercial building flight of stairs) with or without an assistive device. Finally, the timed up and go is a screening test that has high reliability to predict fall risk (28). In this timed test, subjects begin in a seated position in an armchair. They are asked to rise, go forward 3 meters, turn around, and sit back down. A time in excess of 14 seconds indicates a high fall risk in elderly community dwelling ambulators (with and without assistive devices).

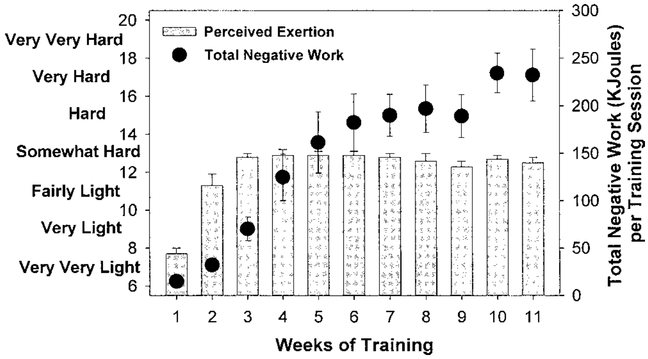

Figure 2. The perceived exertion (gray bars), as reported on the Borg rating of perceived exertion scale, remained relatively low and constant following a 2-week acclimatization period, yet the negative work (black circles) continued to increase >3-fold following the acclimatization. The negative work levels achieved by the end of the study are high for an elderly population. Error bars = 1 *SEM*.

Statistical Analyses

The statistical analyses addressed 2 questions relative to the resistance exercise mode. When the question was whether a pre- to post-training effect occurred within a group (ECC vs TRAD) a paired t test was used, but when additional time periods (beyond pre- and post-training) were of interest, a one-way repeated measures analysis of variance (ANOVA) was used. When pre- to post-training comparisons between groups were of interest, a two-way repeated measures ANOVA was employed. Statistical significance was declared with alpha levels <0.05. When significant group by time interactions occurred, a Tukey's pair-wise multiple comparison test was used. Descriptive statistics were also used to better describe effects.

RESULTS

Negative Work, Perceived Exertion, and Muscle Soreness (ECC Group Only)

After the initial progressive increase in the target perceived exertion (weeks 1 and 2), the total negative work more than tripled over the final 9 weeks for the ECC group, during which time there was no clinical change in their perceived exercise exertion ("somewhat hard") (Figure 2). For example, the most frail of the ECC subjects, an 89-year-old subject who depended on a cane at the start of the training for normal locomotion, maintained 216 (negative) watts for 15 minutes, and the least frail maintained a workload in excess of 400 (negative) watts for 20 minutes (and a peak of 444 W for over 10 minutes) by the conclusion of the training. To put these work rates in perspective, the 1-hour cycling record on an oval cycling track is about 440 (positive) watts (31). In addition to a relatively low perceived exertion, all ECC subjects reported this exercise to

Table 1. The Mean Values (With Units) (± 1 *SE*) of the ECC and TRAD Groups Pre and Post 11 Weeks of Resistance Training

	Eccentric Group		Traditional Group	
	Pre-Training	Post-Training	Pre-Training	Post-Training
Strength (N)	48.8 ± 6.07	78.1 ± 8.78*†	45.5 ± 5.48	52.5 ± 4.30
Fiber Area (μm^2)	3295 ± 366	5273 ± 963.5*	2999 ± 313	4218 ± 367*
Timed Up & Go (s)	16.65 ± 0.81	11.96 ± 0.72*†	17.20 ± 0.87	15.55 ± 1.45*
Stair Descent (s)	25.3 ± 2.01	20.9 ± 2.10*†	21.4 ± 2.32	22.9 ± 4.36
Berg Balance	49.7 ± 1.14	53.4 ± 0.64*	42.0 ± 2.38	44.3 ± 1.37

Notes: *Significant differences ($p < .05$) within groups from pre- to post-training; †significant differences ($p < .05$) between groups.
ECC = eccentric; TRAD = traditional.

be "easy and desirable" compared to other resistance exercise modes. Only very little (mean = 1.2 cm out of a possible 15 cm [statistically nonsignificant]) leg muscle soreness was present in the ECC group during the first 3 weeks. For the remaining 8 weeks of ECC training, soreness was essentially absent (statistically nonsignificant)—0.2 cm out of a possible 15 cm.

Quadriceps Muscle Structure and Function

Vastus lateralis muscle fiber cross-sectional area was significantly ($p < .05$) increased in both the ECC and TRAD groups following 11 weeks of resistance training; however, there was no significant differences between the groups. Fiber cross-sectional area (vastus lateralis) in the ECC group increased by 60% and in the TRAD group by 41%. Isometric knee extension strength (which was equivalent in both groups pretraining), however, only increased significantly ($p = .001$) in the ECC group by 60%, while the TRAD group had a nonsignificant ($p = .12$) increase of 15% (Table 1, Figure 3).

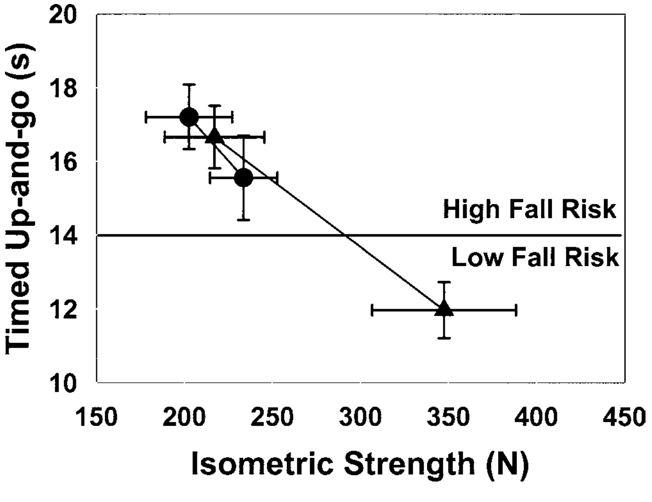

Figure 3. Performance of the subjects (as measured both pre- and post-training) on a task dependent (in part) on leg strength, i.e., the "timed up and go" fall-risk assessment. Any improvement in leg strength in an elderly population likely has a clinical effect. Here the traditional (TRAD) group (circles) clinically improved their strength (15%) and time ($p = .03$) on the fall-risk assessment (1.7 s). The eccentric (ECC) group's (triangles) strength and fall risk, however, though no different than the TRAD group initially, did improve significantly ($p < .05$) in strength (60%) and with the timed up and go (4.7 s). In fact, the larger magnitude increase in strength was coupled to a shift in the ECC group from a high fall risk to a low fall risk following training. Error bars = 1 *SEM*.

Balance, Stair Descent, and Fall-Risk Performance

Performance of the ECC subjects on tasks dependent (in part) on leg strength showed significant ($p < .05$) improvement (Table 1). ECC subject scores on the Berg balance scale improved by 7%, stair descent time improved by 21%, and the ECC subjects went from a high to a low fall risk as measured by their 4.7-second improvement and their crossing the 14-second threshold (high to low fall risk) on the timed up and go (fall risk) evaluation (Figure 3). The TRAD group (which did not differ from the ECC group at the pretraining assessment of the timed up and go) did significantly improve their timed up and go (1.7 s) ($p = .03$), but this was not enough of an improvement to cross the fall-risk threshold. The TRAD group had nonsignificant improvements in balance (5%) ($p = .22$) and stair descent time (7%) ($p = .56$).

Discussion

The most consequential effects of this high muscle force negative work intervention were that the elderly patients (a) tolerated the intervention at a "somewhat hard" perceived exertion level, (b) increased both the size and strength of their quadriceps (vastus lateralis) musculature, (c) all improved their balance and stair descent abilities, and (d), most importantly, their fall risk was reduced from high to low.

Considerable strength gains (upwards of 100–200%) (32–35) and associated improvements in mobility (4,36,37) have been noted, even among the oldest-old, with traditional resistance exercise regimes. We note a 15% clinical improvement (although statistically not significant) in strength, coupled with a modestly improved timed up and go following a traditional resistance exercise regime. Previous studies (5,6,34,38–40) using various forms of resistance exercise with elderly persons have reported similar modest improvements in strength and mobility while reducing the risk of falling. Because even small gains in strength can reduce frailty (41,42), we were curious if these effects on frailty could be amplified with larger strength gains in an elderly population utilizing a negative work intervention.

This report documents that the highest muscle forces possible, i.e., via negative work, cannot only be performed with a tolerable low-to-moderate effort ("somewhat hard") in an at-risk elderly patient population, but can also increase muscle size and strength dramatically while greatly reducing the fall risk. Either weight training or eccentric exercise clinically improved strength and reduced fall risk, the magnitude of each of these was far greater (and significantly different) when the subjects performed negative work with eccentric exercise (Figure 3). We consider this to be one of the most alluring results of this study.

It also is apparent that the significantly increased muscle strength in the ECC group seems to be linked to an equal-magnitude increase in fiber cross-sectional area. Because percutaneous sampling of locomotor muscle is variable, caution must be exerted when interpreting the cross-sectional area findings. There is, however, an apparent coupling of strength and cross-sectional area following high negative work training only, suggesting a likely structural basis to the strength increase. Furthermore, the exposure to chronic bouts of negative work positively influenced their performance skills critical to daily living, balance, and stair-descending abilities (where most falls occur). This can be explained in part because elderly persons have a decreased ability to produce submaximal controlled eccentric contractions (24–27), the exact type of muscle activity used to successfully descend stairs, and these skills may have benefited directly from the negative work training. The timed up and go (fall-risk assessment) task, however, requires a combination of both eccentric and concentric contractions. Therefore, the negative work countermeasure, coupled with the resultant greater force-producing abilities, likely influenced fall risk greatly in the ECC group.

The response to high muscle force negative work in these elderly subjects was identical to that of younger, healthy subjects (19,22). Following a 3-week progressive ramping-up of negative work, both young and old subjects are able to exercise at high average negative work rates without any decrease (rather a large increase) in isometric force production. Also, in both the young and old groups, the increases in muscle strength closely approximate the increases in muscle fiber cross-sectional area (19). It is unclear, however, as to what specific adaptation occurs in the muscle during the progressive ramping of the negative workload, or in the neuromuscular control driving the muscles, to "protect it from soreness." However, the progressive intensification of negative work, despite a constant perceived effort by the subjects, does appear to be essential to avoid injury (10).

Thus, a negative work intervention, because of the high muscle force and low energetic cost attributes, may be ideally suited to those elderly persons that have an impaired ability to deliver oxygen to working locomotor muscles (i.e., exercise-intolerant individuals). Often it is this exercise-intolerant patient population that suffers the greatest decline in muscle strength and subsequent function, usually resulting in a positive feedback loop of downward mobility and often ending in debilitating falls. High-force negative work is an intervention that is tolerated and perceived as only "somewhat hard," but provides a powerful stimulus to muscle growth and strength. Therefore negative work may be an important countermeasure to reverse muscle impairments and loss of independence.

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