Review

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HIGHLIGHTED TOPIC | *Eccentric Exercise*

Eccentric exercise in rehabilitation: safety, feasibility, and application

Paul LaStayo,[1] Robin Marcus,[1] Lee Dibble,[1] Fernando Frajacomo,[2] and Stan Lindstedt[3]

[1]*Department of Physical Therapy, University of Utah, Salt Lake City, Utah;* [2]*Department of Pathology, University of Sao Paulo, Sao Paulo, Brazil; and* [3]*Department of Biology, Northern Arizona University, Flagstaff, Arizona*

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LaStayo P, Marcus R, Dibble L, Frajacomo F, Lindstedt S. Eccentric exercise in rehabilitation: safety, feasibility, and application. *J Appl Physiol* 116: 1426–1434, 2014. First published July 3, 2013; doi:10.1152/japplphysiol.00008.2013.—This nonexhaustive mini-review reports on the application of eccentric exercise in various rehabilitation populations. The two defining properties of eccentric muscle contractions—a potential for high muscle-force production at an energy cost that is uniquely low—are revisited and formatted as exercise countermeasures to muscle atrophy, weakness, and deficits in physical function. Following a dual-phase implementation, eccentric exercise that induces rehabilitation benefits without muscle damage, thereby making it both safe and feasible in rehabilitation, is described. Clinical considerations, algorithms of exercise progression, and suggested modes of eccentric exercise are presented.

eccentric; rehabilitation; muscle; function; patients

LENGTHENING (ECCENTRIC) MUSCLE contractions have received much less experimental attention than either isometric or shortening (concentric) contractions, especially in rehabilitation populations. However, they have had an interesting and at times curious research history. Our current understanding of muscle energetics is often and appropriately traced to A. V. Hill and his brilliant student, D. R. Bassett Jr. (9). Another one of Hill's students, W. O. Fenn (28), focused on muscle energetics in general and the energy "cost" of doing work, in particular. What is now known as the "Fenn Effect" is a recognition that the energy cost of muscle contraction is roughly equal to the cost of force production, plus the additional cost of the work produced. In other words, the energy required for force production in skeletal muscle is increased when muscles shorten while contracting and doing positive work (91). However, Fenn (28) also made an observation that received far less attention, namely, that if a muscle is stretched while contracting, the energy liberated by the muscle is reduced. We could call this a "Negative Fenn Effect," which led none other than Hill himself to speculate that the identical chemical reactions that consume ATP in shortening contractions could be reversed when muscles are subjected to mechanical stretch ("negative work") during lengthening contractions, functionally generating ATP (49, 50). Whereas this "ATP generation" concept has been debunked long ago, these early experiments first established that the energy cost of isometric force production is: *1*) increased if work is done by the muscle and *2*) reduced if work is done on the muscle (eccentrically induced negative work). Thus these early studies established that the energy cost to produce identical magnitude and duration of force is least during eccentric contractions.

In addition to their low-energy cost of force production, eccentric contractions generate the highest forces. Nearly one and one-half centuries ago and long before the contributions of A. V. Hill, Adolf Ficksee Fick (29) published a paper that first: *1*) introduced the term "isometric" to denote a muscle contraction in which no change in length occurs and *2*) documented that if a muscle were stretched during a contraction, it could produce increased force. The enhancement of force production during stretch in muscle has remained a curious observation with uncertain mechanistic explanations, even with the introduction of the sliding filament theory (52, 53). Recently, the magnitude and cause of this stretch enhancement in force are receiving increased attention (22, 46). In fact, the behavior of muscle during stretch has generated a new addition to the sliding filament model of muscle contraction, where force enhancement is generated by the "engagement" of passive structural elements (e.g., titin) upon activation (44, 83). Whereas there remains some debate regarding causation, there is no debate that skeletal muscle can produce far greater force if stretched while activated, i.e., during an eccentric contraction, than it can during either an isometric or concentric contraction.

Thus the two defining properties of eccentric muscle contractions have been known for nearly one century: *1*) force production is uniquely high, and *2*) energy cost to produce the force is uniquely low (70, 71, 92). Over 40 years ago, the observation was made by Komi and Buskirk (58) that because of these defining properties, eccentric exercise has the greatest potential for muscle training or "conditioning." Indeed, high force and low cost constitute ideal characteristics for resistance exercise interventions designed for rehabilitation populations. Many frail or otherwise exercise-limited individuals (e.g., those suffering from chronic cardiac or obstructive pulmonary diseases, cancer, or metabolic, neurologic, or postoperative conditions) are impaired in

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Address for reprint requests and other correspondence: P. LaStayo, Dept. of Physical Therapy, Univ. of Utah, Salt Lake City, UT 84112 (e-mail: paul.lastayo@health.utah.edu).

their abilities to produce sufficient muscle force to preserve their muscle mass and function, and/or they lack the energy capacity to do so. Even modest exercise interventions may be beyond their capabilities. Without sufficient load on their muscles, they enter a downward spiral of muscle wasting, often resulting in life-threatening falls. Thus interventions for these individuals are needed that can produce high force but do so with minimal energetic cost.

Despite their alluring characteristics, eccentric contractions of muscle have been viewed more as an anomaly rather than a potential life-enhancing intervention. The reason stems from another association with eccentric contractions—muscle damage. As eccentric muscle contractions became so linked with delayed-onset muscle soreness (6, 21), they are now the primary experimental tool for causing and studying muscle damage. A quick PubMed search coupling "eccentric" with "injury or damage" yields over 1,000 citations but less than 50 if coupled with "rehabilitation or beneficial." This association has become so strong that eccentric contractions are often viewed as inevitably linked to muscle damage. Perhaps because of the very high forces that can be generated eccentrically, it is not surprising that they can cause muscle damage (6). Indeed, there has been a persistent idea that damage is a necessary prerequisite for any muscle remodeling (21, 26, 30, 102). If always true, this would be a very unfortunate constraint for rehabilitation, because those individuals who could benefit most from increased muscle strength are often those with the greatest vulnerability to any inflammatory response (36, 112).

Evidence is now mounting that muscle damage is neither inevitable nor necessary for muscle rehabilitation. First, evidence exists that eccentric exercise training can be used safely and effectively in rehabilitation (17, 19, 34, 62). The single key in avoiding any adverse muscle response of damage or injury to the muscle is dose. When high eccentric forces are generated in muscle that is naive to eccentric contractions, damage is almost inevitable. However, if the magnitude and duration of the force production are increased gradually over time, no symptoms of damage, inflammation, or even soreness are present (61, 65). Second, the beneficial muscle structure and function responses can occur completely independent of any observable symptoms of muscle inflammation or injury (30). Thus the use of high-force eccentric contractions to promote muscle rehabilitation, with no detectable damage, has great potential (51).

In this mini-review, we discuss the use of chronic eccentric training as a resistance exercise intervention for rehabilitation populations (Fig. 1). The rehabilitation focus is directed to adults or older adults with comorbid disease conditions and/or adults or older adults recovering from surgery and joint injury. The groups described are diagnostically diverse, although the common impairments of muscle atrophy and weakness underlie (in part) their deficits in physical function.

SAFETY AND FEASIBILITY IN REHABILITATION POPULATIONS

Diverse samples of individuals in rehabilitation programs have demonstrated the ability to safely progress negative work over a course of many weeks of eccentric exercise training (17, 32, 33, 61, 62, 69, 75, 76, 97). Importantly, to safely progress negative work, a segue from an adaptation phase to a phase that uses higher doses of eccentrically induced negative work is required to avoid unnecessary muscle damage and negate the possibility of adverse responses, which include profound pain, weakness, and at worst, exertional rhabdomyolysis (101). In contrast, eccentric exercise implemented chronically to reverse tendinopathies is often designed to induce a pain response as part of the therapeutic regimen [note: this approach is covered in detail in the previous paper in this mini-review by Kjaer and Heinemeier (55a) and will not be covered here]. Moreover, in older adults and populations plagued by disease and/or recovering from surgery, a phased-in progression of nonpainful nor injurious eccentric exercise has been shown to be universally feasible, since the relative exertion required to perform increasing amounts of negative work is low. Additionally, peak heart rate, systolic blood pressure, cardiac index, and expired ventilation in older adults are lower during eccentric bouts of exercise of equivalent volume to concentric exercise (59, 110). Consequently, high levels of adherence and compliance with eccentric exercise have been reported (75, 79, 90).

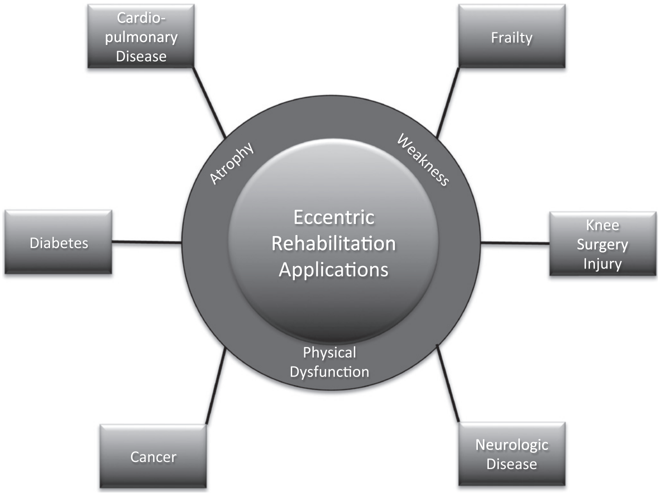

Fig. 1. Eccentric rehabilitation applications for individuals with a variety of age and/or medical-related conditions, all of which share muscle atrophy, weakness, and physical dysfunction as common impairments.

Older adults. Older adults in rehabilitation settings, including individuals characterized as frail, can partake in eccentric exercise without signs or symptoms of muscle or joint injury. Older adults living with diseases that result in atrophy, fatigue, and weakness can progressively load their locomotor muscles eccentrically without inducing classic damage responses, such as increases in creatine kinase and/or inflammatory markers, along with decrements in force production (17, 60, 75). Negative work increases of approximately two- to tenfold (17, 33, 35, 61, 62, 75) over a course of 10–12 wk are attainable with this population and may underlie the promotion of growth factors and molecular changes consistent with a positive muscle response to resistance exercise (60, 75, 81, 115). Furthermore, since the perceived exertion required to produce these high levels of negative work are only "somewhat hard," older adults appear more willing to attend a high fraction (>90%) of the two to three times/wk eccentric rehabilitation over a course of 6–12 wk. Meticulous attention to proper positioning, alignment, and form is necessary to avoid undue stress on the ankle, knee, and hip joints during eccentric exercise, especially in those with osteopenia and or osteoarthritis. After each session of eccentric exercise, older adults may experience an acute bout of leg fatigue, so a short rest period may be warranted before moving on to any other exercise modes.

Adults with cardiopulmonary disorders. Individuals with coronary artery, chronic heart failure, or chronic obstructive pulmonary disease typically have cardiac and/or ventilatory restrictions that can constrain exercising in rehabilitation programs. In principle, eccentric exercise can be an attractive and feasible alternative to resistance exercise for patients with limited cardiopulmonary exercise tolerance. When exercising eccentrically, adults and older adults with minimal left ventricular dysfunction and no exertional ischemia can produce fourfold greater muscular stress and induce improvement in the distance walked in 6 min without overstressing the cardiovascular system, i.e., at cardiovascular and metabolic levels similar to those observed during concentric exercise (11, 79). Similarly, those with severe chronic airway obstruction, e.g., forced expiratory volume <50% predicted, have achieved nondamaging, high negative work levels during eccentric ergometry exercise with tolerable levels of leg fatigue and dyspnea compared with concentric ergometry exercise (97). Standard cardiopulmonary rehabilitation exercise-monitoring precautions should be used during eccentric exercise with this population.

Older adults who have survived cancer. Survivors of cancer and its treatment often experience a reduced quality of life, due, in part, to impaired muscular abilities and deficits in mobility. Many older adults who survive and are considered anabolically impaired can still feasibly exercise using eccentric contractions. Older (average age of 75 yr) adult survivors of breast, prostate, or colorectal cancer participated in 34 out of 36 eccentric exercise sessions over 12 wk and increased their negative work more than threefold without a muscle-injury response (62). Despite hormone-related, muscle-function deficits, survivors of prostate cancer on androgen deprivation therapy are able to exercise adequately to derive benefits in strength, mobility, and fatigue levels in an eccentric exercise rehabilitation program (40). There has not yet been any reported exacerbation of cancer-related fatigue following eccentric exercise, although this should be monitored closely, especially immediately following an exercise bout. Furthermore, any cancer-related treatments that might impair immune response or amplify catabolic processes of older adults will require close attention and care so as not to amplify these adverse responses to treatment.

Adults with metabolic conditions. Adults with type 2 diabetes can experience an acceleration of muscle loss, especially when coupled with increasing age (84). Loss of muscle strength is also greater in older adults with diabetes relative to their peers (85), and this is, in part, likely related to the increased fall risk seen in this population (77, 103, 111). Exercise aimed at improving muscle mass and strength in persons with diabetes is now recommended regularly (4a, 12a, 105). Whereas a single exposure to eccentric resistance exercise specifically has been associated with increased insulin resistance (7, 55, 86) and a parallel skeletal muscle-damage response, more recent evidence (37) suggests that elevated glucose and insulin responses to an oral glucose tolerance test in healthy, young women, after an initial bout of eccentric exercise, are attenuated after a repeated eccentric bout, and after chronic exposure to eccentric training (86). With skeletal muscle, accounting for nearly 80% of glucose uptake, it is important to exercise the locomotor muscle in metabolically impaired populations without worsening insulin resistance. Chronic and progressive exposure to eccentric exercise results in significant improvements in leg lean mass, strength, and mobility, without adversely impacting insulin sensitivity in overweight, physically inactive, postmenopausal women with impaired glucose tolerance (74) and has been shown to enhance insulin sensitivity and decrease glycosylated hemoglobin by 10.6% in young, sedentary women (86). Furthermore, in healthy, sedentary adults (mean age 48 yr), chronic exposure (8 wk, three to five times/wk) to downhill hiking—a predominantly eccentric exercise modality—has also been shown to be similarly, metabolically beneficial to concentric exercise (uphill hiking) (20, 114). Importantly, these metabolic improvements were accompanied by decreases in two typical markers of muscle injury: high-sensitivity C-reactive protein and serum creatine kinase. Because adults with diabetes often suffer from diabetes-related micro- and macrovascular complications, including cardiovascular disease, retinopathy, peripheral neuropathy, and peripheral vascular disease, eccentric resistance exercise presents a viable alternative or adjunct to more traditional resistance or aerobic exercise in this population. Eccentric exercise, in particular, because of its lower energetic cost and perceived exertion, is safe and feasible for those with diabetes (73, 75). If, however, the goal of rehabilitation is to use more energy during rehabilitation and decrease weight and body mass index, the lower metabolic cost of eccentric exercise may not be an ideal intervention and should be coupled with aerobic exercise (75). To maximize safety, techniques to minimize valsalva should be used, and visual foot inspections should be performed regularly. Glycemic responses to resistance training, especially hypoglycemia, should be monitored closely, as should changes in diabetes medications.

Adults and children with neurologic conditions. Individuals with central or peripheral nervous system deficits not only experience peripheral muscle atrophy but also a constrained, or lack of, neural drive to the muscle. The combined effect of these deficits may greatly restrict the force-production ability of skeletal muscle and therefore, impair mobility. It has been suggested that this loss of muscle function is obligate to central nervous system conditions; however, recent research, using concentric or eccentric training, suggests otherwise (14, 16, 27, 39, 56, 78, 106). Preliminary evidence in a limited number of central nervous system disorders suggests that eccentric training is a safe and feasible means of providing resistance exercise (17, 42, 94). For example, no sustained increase in markers of muscle damage or loss of isometric force production was noted during a 12-wk, high-intensity eccentric training program in mild to moderately impaired older adults with Parkinson's disease (17). Furthermore, older adults following a stroke can improve leg muscle power with both standard and eccentric resistance training; however, greater cross-education effects have been noted in the nonparetic (untrained) legs only following high-intensity eccentric rehabilitation. This suggests that eccentric training may be inducing central neural adaptations (14). One concern regarding eccentric contractions in persons with upper motor-neuron lesions is the potential to increase spastic muscle responses due to lengthening of muscle in the context of hyperactive stretch reflexes. To our knowledge, few studies have addressed this issue experimentally;

however, a recent study in children who exercised eccentrically has attenuated this concern. In children with cerebral palsy and upper-limb spasticity, eccentric strength training resulted in increased torque throughout range of motion, as well as reductions in electromyography-measured co-contractions (94).

Resistance training in the context of peripheral nervous system and neuromuscular disorders has historically been more controversial. Unfortunately, the specific effects of eccentric training cannot be determined from these studies, since the descriptions of the resistance training interventions suggest a combination of concentric and eccentric contractions. Certainly more research is needed to understand the effects of eccentric training in these disorders.

Adults following orthopedic knee surgery or joint injury. The early postoperative period following both anterior cruciate ligament reconstruction and total knee arthroplasty is the typical period for amplified muscle (e.g., the quadriceps) atrophy and weakness. The establishment of safety and feasibility is of utmost importance to any intervention applied after these surgical procedures. Foremost is the need to retain the stability afforded by the ligament reconstruction by closely monitoring the intensity of the resistance exercise and any adverse joint responses. Pain, knee effusion, injury recurrence, and instability rates are important metrics underlying knee-joint safety following knee surgery. If the eccentric rehabilitation is judiciously implemented and progressed, as outlined in the series of papers by Gerber et al. (32, 33, 35) and reviewed by Lepley and Palmieri-Smith (68), the knee stability is not compromised following anterior cruciate ligament reconstruction in those with either patellar tendon or semitendinosus-gracilis grafts (32). No differences in any of the safety measures mentioned above have been noted following 12 wk of rehabilitation with eccentric exercise as the resistance mode vs. accelerated rehabilitation with standard resistance exercise, initiated 3 wk after surgery (32). The successful progression of negative work over a course of many weeks of rehabilitation suggests that eccentric exercise is also feasible. Eccentric exercise, 3 wk after total knee arthroplasty surgery, also does not adversely impact joint or muscle responses, despite a fivefold increase in negative work over 6 wk (76). Similar findings have been noted when implementing eccentric exercise many months following operative and nonoperative eccentric rehabilitation for musculoskeletal knee-joint injuries (38). Clearly, any adverse joint responses, such as an increase in knee-joint swelling or a loss of knee-joint range of motion, would be an indication to discontinue eccentric exercise. What has been reported to date suggests that knee swelling can be avoided, and knee range of motion increases with eccentric exercise after surgery (15, 38, 64, 76). Therefore, the early safe and feasible implementation of eccentric exercise as part of knee rehabilitation should be considered safe, and the reported >85% adherence is added evidence of its feasibility.

ECCENTRIC REHABILITATION: MUSCLE AND PHYSICAL FUNCTION OUTCOMES

Given the safety and feasibility of eccentric exercise and the high-force, low-cost nature of negative work, the application of eccentric resistance exercise as a strength training intervention to counteract sarcopenia and postoperative muscle atrophy in rehabilitation populations is alluring. Sarcopenia has historically been defined as a loss of muscle mass, although more contemporary and clinically applicable definitions include the loss of muscle strength and mobility.

Numerous gaps in our mechanistic understanding, following chronic eccentric training, exist; however, proposed mechanisms attempting to explain preserved eccentric force capacity in older individuals, how force enhancement following active muscle lengthening occurs, and changes underlying a protective repeated bout effect may also be appropriate explanations for changes following eccentric rehabilitation. Whereas classic hypertrophic-signaling responses to resistance training may explain, in part, how enhanced function follows eccentric training, these typical responses do not account for all of the changes. Several other neurologic, mechanical, and/or cellular adaptations have been proposed (98). Examples of such are heightened quadriceps stretch-reflex activity in adults surviving a stroke and an enhanced neural drive with eccentric training (25); a higher contribution of synergistic muscle and cross-educational effects associated with central neural adaptations (14, 87); a mechanical stress-dependent increase in the proportion of attached cross-bridges with eccentric activity (45, 66); and a change in the use of passive elements in the muscle cells, such as titin (67, 80), and elastic elements transmitting force outside of the cell, such as the tendon (95, 96).

These proposed mechanisms of adaptation will not be particularly helpful for the clinician in designing eccentric rehabilitation protocols, although they do highlight the need for a more basic understanding of how the following changes occur. Here, below, we briefly review the impact of eccentric rehabilitation trials aimed at halting or reversing sarcopenia and postoperative atrophy in rehabilitation populations.

Muscle size. Muscle hypertrophic responses following eccentric resistance exercise, measured at the fiber- and whole-muscle level, are mixed. Hypertrophy, following eccentric exercise in older adults, is greater (90) or equivalent (82, 90, 93) to that following standard resistance exercise. Other structural changes synonymous with positive responses following resistance exercise can occur. For example, increased vastus lateralis thickness (90) and decreased depots of leg intramuscular fat (75, 81, 82) have been demonstrated in older adults.

Following total knee arthroplasty (15, 64, 76) or when aging is coupled with disease, e.g., cardiopulmonary, cancer, diabetes, or Parkinson's disease, a more predictable increase in muscle size occurs (18, 63, 75, 107). The greatest changes in leg muscle cross-sectional area or volume have been reported in adults following anterior cruciate ligament reconstruction (12, 32, 33, 35). Importantly, from a rehabilitation perspective, these changes can occur when eccentric exercise is initiated, 3 wk after surgery and continued for 12 wk. This may be due to the fact that this rehabilitation population is typically younger and less impacted by impaired muscle-growth responses that hinder older, diseased rehabilitation populations. The increase in the volume of the quadriceps and gluteus maximus muscles has been observed to be twice that following the standard accelerated ligament reconstruction rehabilitation program (33). Additionally, these greater muscle responses can be maintained and coupled with functional strength and hopping improvements, 9 mo following eccentric rehabilitation (32). Similarly, greater increases in quadriceps muscle volume have been noted in older adults, 1–4 yr after their total knee arthroplasty surgery (64) and in older adults with Parkinson's disease (18) when eccentric resistance exercise is incorporated in a rehabilitation program compared with standard resistance exercise.

Additionally, older adults characterized as anabolically impaired, such as survivors of cancer (63) or postmenopausal women with impaired glucose tolerance (74), can grow muscle following eccentric exercise compared with standard-care approaches. The magnitude of improvement, however, is less than in those who are not anabolically impaired. Rehabilitation with eccentric exercise for those in their fifth decade demonstrates mixed-muscle hypertrophy responses. Adults with type 2 diabetes mellitus demonstrated hypertrophy with a program that combined aerobic and eccentric resistance exercise vs. aerobic exercise only (75). Alternatively, those with stable coronary artery disease, however, did not change their quadriceps muscle-fiber area with eccentric exercise (107). Since no studies with rehabilitation populations have compared work- and intensity-matched bouts of isolated eccentric and concentric exercise, the suggestion that contraction type significantly influences hypertrophic signaling and adaptation is still not clear.

Muscle function. Muscle strength and power enhancements appear to be more predictable than changes in muscle size after a course of rehabilitation with eccentric exercise, even when there is no differential increase in muscle size noted in older adults who exercise eccentrically vs. concentrically (61, 82, 107). At times, strength improvements following eccentric exercise in older adults may be superior to (90) or equivalent to (93) improvements noted in a concentric or high-velocity training group (69). These strength improvements occur with all contraction types, although some studies characterize the strength enhancement as muscle contraction-type specific (38, 93). Eccentric exercise training may also assist older adults in tasks that require control of submaximal muscle forces (61, 82, 90). This may be especially important for older adults at high risk of falling, who have been observed to have poorer control of submaximal eccentric muscle forces (88, 89).

Older adults enrolled in cardiopulmonary (79, 97, 107) or postoperative knee (64, 76) rehabilitation can improve muscle strength with eccentric exercise. Furthermore, those exercising eccentrically following a diagnosis of cancer (40, 62, 63), Parkinson's disease (17, 18), polymyositis (41), or osteoarthritis (38) or a metabolic impairment (74) all demonstrate eccentric resistance exercise training effects manifested as improved strength and/or power.

Clinically important and statistically significant increases in strength and strength-related variables have also been noted in nonelderly adult rehabilitation populations. Adults in rehabilitation following anterior cruciate ligament reconstruction (12, 32, 33, 35) highlight the potential for a rapid restoration of strength following eccentric exercise. Smaller strength enhancements have been noted in individuals with isolated insufficiency of their posterior cruciate ligament of the knee (72), those with multiple sclerosis (42), and children with cerebral palsy (94).

Physical function. Improvements in muscle size and strength provide evidence of the physiologic efficacy of eccentric exercise; however, such effects are of little relevance if they do not also produce enhancements in physical function, here defined as the "the ability to move around" (10) and "the ability to perform daily activities" (109). Ubiquitous impairments in muscle structure and function (e.g., composition and strength) underlie the physical function deficits.

This link between muscle strength and mobility performance drives the need for resistance exercise as part of a rehabilitation program in needy adult and older-adult populations (64, 98, 108). Muscles nearly equal amounts of positive and negative work during normal gait and locomotion (13, 43), and many precarious, high fall-risk tasks, such as descending stairs, rely almost exclusively on eccentric muscle contractions. Therefore, it is not surprising that all previous eccentric exercise trials that monitored mobility levels in rehabilitation populations have demonstrated improvements in a wide variety of physical function tasks requiring both eccentric and concentric contractions. The greatest eccentric exercise effects on mobility to date have appeared in individuals following knee surgery (38, 64, 76) or in those with the most to gain (18, 63, 75, 100, 110). Fewer studies using eccentric rehabilitation have documented abilities to perform daily activities, although improvements in self-reported quality of life have been noted in total knee arthroplasty recipients and older individuals with Parkinson's disease (19, 32, 64).

Thus rehabilitation interventions targeting eccentric muscle contractions can benefit older adults requiring rehabilitation, not only to improve their mobility but also to avoid falls, which can improve confidence when moving about. Additionally, even for those not at a high fall risk, the increased reserve of muscle mass, strength/power, and mobility, resulting from eccentric muscle activity, will serve as a physical function "safety factor."

ECCENTRIC REHABILITATION: APPLICATION

Progression of eccentric exercise. To expose patient populations to higher muscle forces using eccentric muscle activity, a progressive ramping of negative work is required. An eccentric exposure-adaptation phase must be implemented initially to avoid unnecessary muscle damage. If a patient's locomotor muscle does not first experience lower eccentric forces and a low volume of negative work during an eccentric exposure-adaptation phase, then the patient typically may experience high levels of muscle damage and consequently, will not adhere to the resistance exercise program nor be capable of experiencing the eventual positive aspects of higher eccentric muscle forces. With the exposure of the muscle to lower doses of negative work initially, an adaptive, repeated bout effect is expected. The mechanisms surrounding this adaptation are multifactorial (47, 48) and beyond the purpose of this mini-review; however, this should not undermine the significant need for this adaptation to occur before higher-dose eccentric loading. When exposing rehabilitation populations to lower doses of negative work during this adaption transient, low levels of delayed-onset muscle soreness are acceptable. Following the eccentric exposure-adaptation phase, the muscle is better prepared to experience the higher forces that are characteristic of a progressive eccentric-negative work phase (Fig. 2).

During the progressive eccentric-negative work phase, the goal is for the rehabilitating participant to resist progressively a higher load for prolonged periods. Eventually, the exercise load being resisted should exceed the participant's isometric maximum load; i.e., the load should now exceed that which can be moved concentrically. The benefit of eccentric resistance

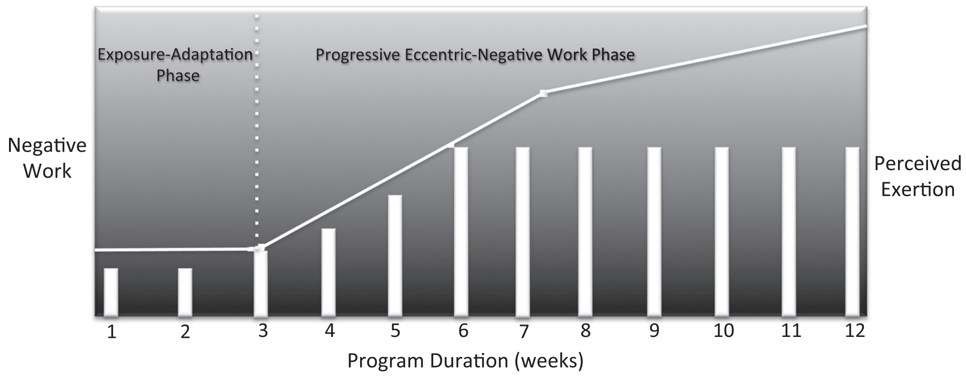

Fig. 2. Sample of eccentric workload progression over 12 wk. *Left* vertical axis and white line: negative work; *right* vertical axis and bars: perceived exertion. Note the distinction (vertical stippled line) between the initial, exposure-adaptation phase, where work and perceived exertion remain relatively stable, and the progressive eccentric-negative work phase, where work and perceived exertion increase in parallel to a point where perceived exertion levels of "somewhat hard" are reached and remain stable while work continues to increase.

exercise from a muscle-strengthening perspective is likely greatest when the exercise load is greater than that which can simply be recovered eccentrically following a concentric component of the exercise (99). In general, the expectation is that the loading goal during the progressive eccentric-negative work phase should exceed an isometric maximum load, and the eccentric exercise duration should be performed for up to 20–30 min/session, two to three times/wk for 6–12 wk (Fig. 3 and Table 1). The use of eccentric ergometry muscle-force output with eccentric contractions has been demonstrated to be up to 1.5 times maximum isometric force (31). With the coupling of this with previous studies (1, 4, 5, 8, 54, 57, 104, 113) that compare eccentric and concentric force, torque, and work, it is not unreasonable to estimate that the total negative work possible/wk could be approximately 20–40% greater than standard resistance exercise, despite similar relative training intensities. This load and ultimate volume of negative work may be best achieved using an eccentric ergometer delivery mode and progressing the intensity using a perceived exertion scale (59).

Modes of eccentric exercise. To implement and experience the muscle and physical function training benefit during the progressive eccentric-negative work phase, external assistance will be required to move the exercise load concentrically before resisting the load eccentrically.

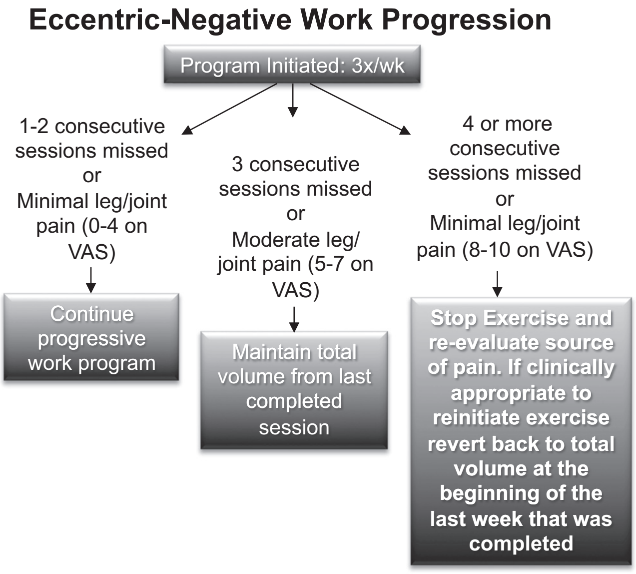

Fig. 3. Eccentric-negative work progression algorithm for temporary pain [visual analog scale (VAS)], adverse reactions, or missed sessions.

In most rehabilitation applications, a motorized ergometer delivers the load to the individual, requiring the exercise participant to absorb energy repeatedly and perform negative work only. Ergometers for both the lower (61, 79, 100) and upper (23, 24) extremities have been described in detail and can be fabricated using motors and controllers. Commercial ergometers (e.g., BTE Technologies, Hanover, MD) are currently available for rehabilitation purposes.

Alternatively, eccentric exercise can be implemented with traditional resistance exercise equipment or with the use of body mass alone. The application of these modes of eccentric resistance requires two extremities to perform the concentric movement, followed by one extremity to perform the eccentric action.

Finally, it is possible to capture the potential benefits of eccentric exercise using an individual's body mass during functional activities (e.g., hiking downhill) or when performing eccentrically biased movement patterns (e.g., Tai Chi). The eccentric loading stems from the individual's body mass, and the activities or movement patterns are designed to transfer progressively more of an individual's body mass over a single leg in an eccentric fashion. With downhill hiking, the knee and hip extensors are performing negative work with each decelerating step. Traditional movement exercise, such as Tai Chi, allows individuals to progress the exercise eccentrically when the hip and knee-flexion range of movement is increased, and/or the speed in which the movements are performed is slowed. Furthermore, functional weight-bearing activities, such as moving from standing to sitting, can be used as an eccentric activity.

Table 1. *Example of progression of total volume of eccentric work on eccentric ergometer over 12 wk*

	Exposure-Adaptation Phase (*weeks 1–2*)	Progressive Eccentric-Negative Work Phase (*weeks 3–12*)
Frequency	2–3×/wk	2–3×/wk
Duration	5–8 min/session	10–12 min/session, *weeks 3–4* 14–16 min/session, *weeks 5–6* 18–20 min/session, *weeks 7–12*
Intensity	"Very light"	"Fairly light," *weeks 3–5* "Somewhat hard," *weeks 6–12*

Duration could be substituted with sets and repetitions of different eccentric exercises.

SUMMARY

Interventions geared toward individuals following surgery or older adults with comorbid clinical pathologies on a progressive downward decline toward mobility limitations and/or frailty (e.g., hip fracture, postoperative, pneumonia) are needed. These interventions are especially important when muscle-mass reserves and quality are low, mobility impairments are high, and physical independence is dwindling. Although pharmacologic approaches are being investigated as alternative methods to increase or attenuate declines in muscle, few if any countermeasures are superior to resistance exercise. The safety, feasibility, and potential clinical benefits of eccentric resistance exercise training regimens for rehabilitation populations are becoming more apparent. In this regard, the further development of parameters to optimize intensity, duration, and modes of eccentric training may lead to significant enhancements in muscle size, strength, physical function, and quality of life for elderly, diseased, or chronically injured individuals.

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DISCLOSURES

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AUTHOR CONTRIBUTIONS

Author contributions: P.L., R.M., L.D., and S.L. conception and design of research; P.L. and R.M. prepared figures; P.L., R.M., L.D., F.F., and S.L. drafted manuscript; P.L., R.M., L.D., F.F., and S.L. edited and revised manuscript; P.L., R.M., L.D., F.F., and S.L. approved final version of manuscript.

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