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Optimizing the Benefits of Exercise on Physical Function in Older Adults

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Abstract

As the number of older adults continues to rise worldwide, the prevention of physical disability among seniors is an increasingly important public health priority. Physical exercise is among the best known methods of preventing disability, but accumulating evidence indicates that considerable variability exists in the responsiveness of older adults to standard training regimens. Accordingly, a need exists to develop tailored interventions to optimize the beneficial effects of exercise on the physical function of older adults at risk for becoming disabled. The present review summarizes the available literature related to the use of adjuvant or alternative strategies intended to enhance the efficacy of exercise in improving the physical function of older adults. Within this work, we also discuss potential future research directions in this area.

1. Introduction

Physical function is an important predictor of health outcomes in older adults. The capacity to perform basic physical functions is a central aspect of health-related quality of life[1] and a key predictor of hospitalization, surgical outcomes, and mortality.[2–5] Accordingly, maintenance of independent functioning is a critical factor in preserving the health and well-being of older adults. In the U.S., nearly half of the 37.3 million persons aged ≥ 65 years report having one or more physical limitations in performing essential daily tasks.[6] The adverse outcomes associated with these limitations have created a significant burden on

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healthcare systems, which is likely to become more substantial given that older adults represent the fastest growing segment of the population.[7,8] As a result, the development of methods to maintain the health and independence of older persons is an important public health goal.

To date, physical exercise is the only intervention consistently demonstrated to attenuate functional decline among seniors (Figure 1).[9–13] Regardless of dependent outcome, most studies in older adults show some degree of benefit to exercise when based on changes in the mean score of a given performance metric. However, these benefits are not observed in all individuals and the change in performance is quite variable.[14] A variety of participant-specific factors may limit gains in functional performance. For example, Manini et al. recently reported that obesity attenuated exercise-induced improvements in physical function among older adults in the Lifestyle Interventions for Independence Pilot Study.[15] In the same cohort, Buford et al. observed that – independent of obesity – participants who took ACE inhibitors derived greater physical benefit from the exercise than non-users.[16] Importantly, each of these findings was independent of differences in confounding characteristics as well as the volume of exercise performed. Accordingly, phenotype (i.e. obesity) and medication use each had significant and yet independent influences on the responsiveness of the participants to training.

These findings suggest that exercise may be necessary, but insufficient, for preserving physical function and preventing disability among many older adults.[17] Consequently, alternative or adjuvant strategies appear necessary to optimize the functional benefits of exercise. While individual studies certainly exist which have evaluated such strategies, a synthesized discussion is needed to demonstrate the tremendous potential of these approaches. The population specificity that may accompany the efficacy of each adjuvant should also be examined. Accordingly, the present manuscript reviews the extant literature related to the efficacy of multimodal and alternative exercise interventions on functional outcomes in older adults and, when data are available, sub-groups of seniors most likely to benefit from these interventions.

2. Pharmacologic administration

In recent years, studies have evaluated the use of pharmacologic agents for the prevention and treatment of age-related sarcopenia (i.e., loss of muscle mass and strength) and functional decline. This approach has the benefit of requiring minimal effort on the part of patients, an important point given that the initial effort required to begin an intervention program is a primary barrier to lifestyle-based treatments.[18] Disappointingly, however, evidence from studies evaluating the effects of mono-modal pharmacologic strategies on physical function have been mixed at best (see discussion below). Despite these equivocal findings, the potential use of pharmacotherapy for improving physical function in older adults should not be abandoned as the efficacy of such medications may be at least partially dependent on the lifestyle habits of the individual. For instance, others have proposed that exercise may stimulate adaptations to pharmaceuticals which are not observed in response to the drug alone.[19] Findings from pre-clinical models provide initial support for this approach. For example, despite showing no effect when given to mice in isolation, an oral PPARδ

agonist increased exercise tolerance when given in conjunction with an exercise training regimen.[20] Thus, the strategy of combining potentially beneficial medications with chronic exercise may be more efficacious than either intervention alone. Here, we briefly discuss the existing evidence and potential utility – in isolation and combined with exercise – of several pharmacologic agents implicated as potential mediators of functional decline.

2.1. Testosterone

Testosterone supplementation has gained interest recently as a possible method for improving physical function and health in older men, evidenced by a 500% increase in the number of testosterone prescriptions over the past several decades.[21] This interest is well-founded considering that testosterone production declines progressively with age[22] and testosterone supplementation may have beneficial effects on body composition.[23–25] Over the past 15 years, numerous studies have evaluated the effects of supplemental testosterone on the body composition and physical function of older men. Despite the strong theoretical basis for potential improvements in function, the evidence to date is inconclusive. Ottenbacher et al. published a meta-analysis focusing on changes in muscle strength in response to testosterone or dihydrotestosterone (DHT) replacement therapy among healthy men 65 years and older.[26] Based on findings from 11 randomized trials, these authors concluded that testosterone/DHT therapy produced a moderate increase in lower-extremity strength; however the effect size (0.63) was dramatically influenced by a single study. Furthermore, the quality of the study design appeared to greatly influence results with lower quality studies reporting larger effect sizes. The same year, Nair et al. published a seminal study on the longer-term (2 years) effects of testosterone supplementation among hypogonadal men aged ≥ 60 years.[27] These authors reported that 5 mg/day of testosterone increased bioavailable testosterone concentrations by 30.4 ng/dL compared to placebo, yet did not result in any significant improvements in physical function. In contrast, Travison et al. recently reported that 6 months of testosterone gel supplementation (10 g/d) improved skeletal muscle strength and stair-climbing power, but not walking speed or self-reported function, in hypogonadal men with mobility limitation.[28] Though speculative, it is possible that the latter study displayed improvements in function due to either the higher dosage of testosterone or because they were already mobility limited. Though evidence regarding the use of testosterone supplementation by hypogonadal, men has been mixed, studies have demonstrated greater efficacy among older men with specific health conditions. For example, authors have reported increases in skeletal muscle mass and strength among older men with HIV infection[29,30] COPD,[31] acute illness,[32] or undergoing chronic glucocorticoid therapy.[33]

Previous research also demonstrates the potential utility of testosterone supplementation when given in conjunction with resistance exercise training. For instance, Casaburi et al. [31] reported that, among men between aged 55–80 years with COPD, the combination intervention induced greater increases in lean body mass and maximum leg press strength than either resistance exercise or testosterone alone. Unfortunately, the authors did not report changes on any additional measures of physical function. Sullivan et al. also investigated the benefits of low- and high-intensity resistance-training protocols for frail men ≥ 65 years of age when completed with or without regular testosterone injections.[34]

These authors found that testosterone injections induced muscle hypertrophy but did not improve muscle strength or functional performance. Additionally, testosterone supplementation did not produce a synergistic interaction with exercise. These authors speculated that the null findings could be at least partially attributable to sub-optimal sensitivity of the functional measures utilized or due to the relatively short intervention duration (12 weeks). However, a another study using a similar 2×2 factorial design reported similar null findings in a middle-aged cohort of HIV+ men.[29]

Despite the strengths of the latter two studies, one important limitation was the relatively small group sizes (n < 20/group) – likely limiting the power to detect interaction effects of interest. Moreover, these studies also utilized weekly injections, rather than daily transdermal, administration of the drug. The route and timing of drug delivery may have also been an important factor in this study's findings. Studies which address these potential limitations may be warranted. Furthermore, studies to evaluate the efficacy of combining testosterone supplementation with other exercise modalities have yet to be conducted. However, the evidence available to date does not suggest that a synergistic effect exists between resistance exercise and testosterone supplementation. Given the potential risks of testosterone supplementation – including increased risk of prostate cancer and cardiovascular events – caution must be used before prescribing testosterone to older men.

2.2 Dehydroepiandrosterone (DHEA)

DHEA, a secretory product of the adrenal gland and a biologic precursor to testosterone, has recently received a tremendous amount of interest as a potential intervention to improve physical function among older adults. DHEA may have advantages over testosterone supplementation in that fewer side effects have been reported and can be safely used by both men and women. Like testosterone, DHEA declines to levels 10% to 20% of the young adult peak by 70 years of age.[35] Because of this decline, scientists have proposed DHEA supplementation as another potential intervention for alleviating various ailments associated with aging. Over the past two decades, research efforts have demonstrated modest beneficial effects of DHEA on body composition, insulin resistance, inflammatory cytokine production, as well as production of insulin-like growth factor one (IGF-1) and testosterone.[36–38] Several studies have also evaluated the relative efficacy of DHEA supplementation for the improvement of skeletal muscle and overall physical function. For instance, O'Donnell et al. reported a positive association between lower circulating DHEA concentrations and performance on a chair stand task among men aged 55–85 years in the Massachusetts Male Aging Study.[39] Conversely, Nair et al. reported that long-term DHEA supplementation had no "physiologically relevant beneficial effects on body composition, physical performance, insulin sensitivity, or quality of life" among men and women aged ≥ 60 years.[27] A recent systematic review of the literature related to the effects DHEA on physical function among persons aged ≥ 50 years indicated that the evidence regarding the utility of DHEA alone was inconclusive as most studies showed no effect of DHEA compared to control.[40] However, only eight studies were included and the studies differed as to whether DHEA was given in isolation or in combination with exercise. Notably, the authors concluded that "studies showing benefit were more likely to include mandatory exercise routines in addition to DHEA supplementation."

To this end, Kenny et al. reported that DHEA supplementation enhanced the efficacy of low-intensity chair aerobics and a yoga program in improving lower-extremity strength and physical function among frail older women.[41] When combined with a twice-weekly exercise program, 50 mg/d of DHEA significantly improved sitting leg press strength and performance on the Short Physical Performance Battery (SPPB) – a validated test of physical function for older adults.[42] Previously, Villareal et al. reported that 6 months of DHEA replacement therapy did not significantly improve strength or muscle mass among older men and women. However, the addition of heavy resistance training resulted in significant gains among the DHEA users compared to placebo.[43] Conversely, Igwebuike et al. reported no additional benefit of 12 weeks of combining DHEA supplementation with exercise compared to exercise alone.[44] Despite the conflicting evidence, the aforementioned studies indicate that DHEA may hold promise as an adjuvant to exercise training for older adults. Future studies are still needed to confirm the safety and utility of this approach.

2.3. Angiotensin-converting-enzyme (ACE) inhibitors

ACE inhibitors are a class of anti-hypertensive drugs that lower blood pressure by blocking the conversion of angiotensin I to angiotensin II and inhibiting the degradation of bradykinin, a potent vasodilatory substance. These drugs have received much attention in recent years regarding their effects that are independent of blood pressure regulation, such as increases in circulating IGF-1.[45,46] In particular, interest has been high regarding the potential utility of ACE inhibitors as therapeutic agents for preventing sarcopenia and functional decline.[47,48] Epidemiologic evidence from the Women's Health and Aging Study and the Systematic Assessment of Geriatric drug use via Epidemiology Study indicated that, compared to non-users, seniors using ACE inhibitors displayed attenuated declines in walking speed and fewer limitations in Activities of Daily Living (ADL).[49,50] Other epidemiologic evidence suggested that these outcomes may have been due to attenuated declines in skeletal muscle mass and strength.[49,51] Despite these promising findings, the results of subsequent randomized controlled trials (RCTs) have been mixed regarding the impact of ACE inhibitor use on functional decline.[52–55] Thus, the benefits of ACE inhibitors on functional outcomes may be limited when utilized as an isolated treatment.

Notably, Carter et al. previously reported that the combination of aerobic exercise and the ACE inhibitor enalapril improved exercise tolerance among aged rats more than either treatment alone.[56] The enhancement of exercise tolerance by ACE inhibition appears to stem at least partially from local skeletal muscle changes. Evidence among older rats indicates that the addition of perindopril to treadmill running results in significant increases in muscle capillary density and the proportion of type I fibers compared to either treatment alone.[57,58] These findings add to an extensive literature from genetic studies in humans demonstrating an important interaction between the renin-angiotensin system and exercise training.[59–64]

Recently, Buford et al. reported that older adults (age ≥ 70 years) who took ACE inhibitors displayed significant improvements in physical function in response to a 12-month exercise program compared to peers who did not take these medications.[16] These findings indicated that the combination of exercise and ACE inhibitor use resulted in dramatic improvements

in walking speed – an important indicator of clinical outcomes in older adults.[3–5] In addition, ACE inhibitor users also demonstrated a significantly greater improvement in performance on the SPPB. Notably, the inclusion of numerous covariates in the primary analysis and sensitivity analyses suggested that these effects were not due to potential confounding variables such as age, gender, and co-morbid conditions. However, residual confounding remains a possibility creating the need for a RCT to evaluate the true effect of combining ACE inhibitor use with exercise.

3. Nutritional modification

Nutritional modification or supplementation has also been widely evaluated as a potential intervention for the prevention or treatment of age-related physical impairments. Though the list of potential dietary- or nutraceutical-based interventions is extensive and many have demonstrated limited efficacy, a few select interventions have shown at least some level of promise. Below we review the potential utility of three such interventions – protein supplementation, dietary restriction, and creatine supplementation – in enhancing the efficacy of exercise for improving the physical function of older adults.

3.1 Protein Supplementation

Protein intake is important for maintaining and enhancing muscle mass, and has been proposed as a potential valuable adjuvant to resistance training. Empirical findings illustrate that resistance exercise alone represents an effective strategy for increasing skeletal muscle mass and strength among older adults.[65–67] In the absence of proper nutritional intake, however, the beneficial effects of resistance exercise are often suboptimal. Acute bouts of resistance exercise indeed stimulate muscle protein synthesis,[68] but in the absence of post-exercise feeding, myofibrillar synthesis is minimized due to concomitant increases in protein degradation.[69] Extensive evidence has demonstrated that ingestion of protein – particularly from sources containing high doses of essential amino acids – is critical to maximizing the accretion of myofibrillar protein among healthy older adults following resistance exercise.[70] As such, this strategy would appear to be critical for maximizing increases in muscle mass and strength following training.

The longer-term utility of protein supplementation, however, remains somewhat in question. Age-related impairments in rates of muscle protein synthesis rates have been reported in a variety of situations including the basal state,[71] following acute ingestion of amino acids,[72] following acute resistance exercise,[73,74] and following short-term training.[75] Given these findings, it seems plausible that supplemental protein intake would help to alleviate impairments in protein accretion by providing additional amino acids from which to synthesize myofibrillar protein. However, aging has also been reported to impair muscle protein anabolism following resistance exercise even when combined with significant amino acid ingestion.[76–78] Meanwhile, other evidence suggests that anabolic responses to post-exercise protein intake may not completely blunted but rather just delayed.[79,80] As a result of these mixed findings, questions remain regarding whether protein supplementation can truly maximize gains in muscle strength and physical function by older adults following resistance training.

Campbell and Leidy compiled data from 106 men and women aged 50–80 years and concluded that resistance training-induced changes in muscle strength and size were not enhanced by dietary protein intakes greater than the American Dietetic Association recommendation of 0.8 g/kg/day.[81] Similarly, a more recent study indicated that supplementation with fortified milk did not enhance resistance training adaptations among 180 middle-aged and older (50–79 yr) men.[82] Despite the strengths of these studies, timing of protein ingestion or feeding was not taken into account, which may have reduced the effect of the treatment on the adaptive responses to long-term resistance training. Esmarck et al.[83] reported that the timing of protein intake after resistance exercise influences the potential for skeletal muscle hypertrophy following exercise training in older people. These authors reported that older men (74±1 yr) who consumed a protein supplement (10 g protein, 100 kcal energy) immediately after resistance exercise experienced increases in whole body fat-free mass, cross-sectional area of the quadriceps femoris, and mean fiber area of the vastus lateralis following 12 weeks of training. Meanwhile, men who consumed the same supplement two hours after exercising experienced blunted responses. However, improvements in strength were similar between groups. This finding may reflect the fact that gains in muscle strength experienced in the first weeks of training by previously sedentary individuals are largely driven by neural influences.[84] This finding agrees with those from other relatively short-term studies indicating no supplemental benefit of post-exercise protein ingestion on muscle strength among older adults with adequate dietary protein intakes.[85–90] As a result, longer-term studies are needed to determine if these increases in lean mass translate to greater improvements in strength and overall physical function.

The optimal dose of post-exercise protein intake also remains a matter of debate. Recently, Yang et al. reported that post-exercise rates of muscle protein synthesis were maximized in young adults by consuming ~20 g of whey protein immediately after exercise.[91] In contrast, 40 g of protein were needed to maximally stimulate myofibrillar protein synthesis among older adults. These results are similar to another report which indicated a dose-dependent response of muscle protein synthesis in middle-aged (59±2 yr) men following resistance exercise and pre-exercise ingestion of beef protein.[92] Notably, the latter report demonstrated that higher doses of beef protein induced greater muscle oxidation of leucine. This finding is in agreement with prior research indicating that increasing the proportion of leucine in the post-exercise meal is necessary to enhance muscle protein synthesis among older adults. Although at least one contrasting report exists,[93] these findings in aggregate suggest that higher doses of protein – with particular emphasis on leucine concentrations – stimulate post-exercise muscle protein synthesis among older adults to a similar degree as that observed for younger adults at lower doses of protein intake.

Despite the extensive prior work in this area, until recently few studies of older adults evaluated the effects of combining resistance exercise with protein supplementation on measures of physical function other than muscle strength (e.g. SPPB, walking speed, Timed Up and Go test, etc.). To our knowledge, four recent trials (N = 60, 65, 80, 161) have evaluated the impact of the combined intervention in seniors using a range of protein intakes from 15–40 g/day for either three or six months duration.[89,94–96] Although one study indicated a significant increase in lean mass by adding protein supplementation (30 g) to resistance training,[96], all four studies indicated that supplemental protein did not enhance

gains in physical function experienced by older adults in response to resistance training. Thus, despite the significant interest in this area, at present it does not appear that supplemental protein is likely to enhance functional performance among seniors who already consume adequate protein in their diet.

3.2 Dietary Restriction

Because the force required to the move the body increases as one become heavier, excess body mass is one of primary barriers to functional improvements among seniors. As such, interventions designed to create caloric (energy) deficits to reduce body mass and potentially improve function have received much attention in recent years. Previous studies suggest that dietary restriction alone is effective in enhancing physical function in older adults with a body mass index (BMI) in the obese range (≥ 30 kg/m^2).[98] Indeed, strong evidence indicates that the reduction in mechanical load placed on joints and muscles following diet-induced weight loss leads to functional improvements, with larger weight losses reducing maximum knee compressive forces to a greater extent than smaller weight losses.[99] Additional evidence suggests that combining dietary restriction with aerobic exercise training appears to produce even larger improvements in physical function compared to either intervention alone.[100]

Despite prior work demonstrating the efficacy of dietary restriction among obese older adults, the practice of such an approach by older adults remains somewhat controversial. Specifically, serious concern exists that weight loss could accelerate sarcopenia and thereby have adverse effects on physical function.[101,102] A relatively large proportion of fat free mass (25%) is typically lost following lifestyle interventions, which combine dietary restriction and exercise training.[103] However, recent clinical trials suggest that the addition of resistance training to a diet plus aerobic exercise program can attenuate the loss of skeletal muscle during weight loss by older adults.[104] Diet plus supervised resistance and aerobic exercise regimens have also been found to substantially improve walking speed and other measures of physical function in obese, older adults.[98,105]

Less is known regarding the effects of dietary restriction on changes in physical function among older adults whose BMI falls in the “healthy” or “overweight” ranges (20.0 – 29.9 kg/m^2). Recent animal studies suggest that dietary restriction may produce health benefits that include reduced body mass and whole-body fat mass, as well as improvements in “biomarkers of aging” (i.e., fasting insulin level, core body temperature).[106,107] However, until further evidence becomes available from humans, the use of dietary restriction as an adjunct intervention to enhance the effects of exercise training should be limited to obese older adults due to concerns related to the potential loss of muscle mass as stated above.

3.3 Creatine Supplementation

Creatine monohydrate (CrM) has been studied extensively over the past 20 years as a nutritional supplement and ergogenic aid for athletes.[108109–111] Previously, a loading dose of CrM was shown to significantly increase phosphocreatine (PCr) resynthesis following intense muscle contractions.[112] This improvement in PCr resynthesis rates is thought to contribute to positive improvements in body composition, muscle strength, and exercise

performance reported when combining creatine supplementation with exercise training.[109,113–115]

Because of the potential to improve adaptations to exercise, Tarnopolsky was among the first to postulate that CrM supplementation may be a beneficial therapy for older adults.[121] Theoretically, an increase in intramuscular creatine (i.e., PCr and free creatine) and corresponding increase in the rate of PCr resynthesis may enable older adults to train at a higher relative intensity and subsequently enhance muscular adaptations. Previously, Chrusch et al. reported that 12 weeks of CrM supplementation significantly increased resistance-training derived increases in whole-body lean mass and lower-body muscle strength among older (mean age: 70 yr) men.[122] Soon after, Brose et al. reported that combining resistance training and CrM supplementation for 14 weeks increased lean mass and isometric leg extensor strength among 28 healthy men and women aged > 65 years.[123] Though an exhaustive list of the potential cellular adaptions underlying this response is beyond the scope of this discussion, these changes may be at least partially mediated by increases in satellite cell number and total myonuclear number observed in response to combining CrM supplementation with resistance training.[124]

Two more recent studies further support the possibility that CrM improves resistance training adaptations among seniors,[125,126] though interpretation of these studies' findings is more difficult because the CrM supplement included another nutrient (i.e. protein; conjugated linoleic acid). Still, despite this challenge and the fact that at least one discrepant report exists,[90] the available evidence appears to support a potential additive or synergistic effect of combining CrM supplementation with resistance training for improving lean mass and muscle strength among older adults. Despite these promising findings, studies are lacking which demonstrate significant improvements in clinical measures of physical function. Accordingly, studies to investigate this potential benefit are warranted.

4. Mechanical Adjuvants

As discussed previously, skeletal muscle strength and endurance are critical factors in maintaining health and independent living among seniors. To date, performance of high-intensity resistance exercise has been demonstrated to be the most efficacious method of maintaining skeletal muscle function. As such, the American College of Sports Medicine recommends that individuals train at or above 65% of 1 repetition maximum (1RM) to achieve muscle hypertrophy and strength gains.[127] However, high-intensity resistance exercise may be difficult for some groups of older adults, including those with musculoskeletal or neurologic impairments. Furthermore, limited self-efficacy often prevents these persons from engaging in high-intensity resistance exercise.[18] Thus, a need exists to develop alternative and/or adjuvant interventions which can maintain skeletal muscle function while utilizing lower-intensity loads.

4.1 Electromyostimulation

Electromyostimulation (EMS) is an established technology that is widely used in sports science. In practice, EMS may use either local or whole-body techniques, or with a combination of the two. Briefly, local EMS delivers impulses that are transmitted through

electrodes on the skin close to a defined group of muscles in order to stimulate muscle contraction.[128] Whole-body EMS (WBEMS), on the other hand, stimulates several muscle groups simultaneously via an electrode belt system.[129] Given the observed physiological benefits of EMS technology in healthy, younger subjects, utilizing such technology in older individuals may provide a safe and effective alternative to combating sarcopenia by increasing or maintaining muscle mass and function.

Despite the potential utility of this modality, few studies to date have examined its efficacy among older adults. Caggiano and colleagues[130] reported a similar improvement in isometric muscle torque production of the quadriceps femoris following 12 sessions of voluntary isometric contraction or EMS in apparently healthy older males (72±4 years). In women aged 62–75 years, Pillard et al.[131] observed a comparable improvement in isometric and isokinetic strength of the lower limbs and vertical jump height following four activity sessions for six weeks of either EMS of the quadriceps, up-and-down stair climbing exercises, or a combination of the two programs. Interestingly, there was greater benefit in bone mineral density and dynamic muscle strength from the superimposed EMS group compared with the other two programs alone. However, none of the three programs altered body composition or posture. Recently, the effects of 6 weeks of EMS superimposed over voluntary contraction training were examined on steadiness in muscle force production of the knee extensors and flexors in persons aged 60–77 years.[132] This training was effective in increasing maximal voluntary muscle strength and in reducing force fluctuation in knee extensor isometric contractions at low torque levels. Accordingly, EMS may contribute to an improvement in force control. However, several limitations to the study – including measurement of maximal voluntary contraction and steadiness at a single knee joint angle of 90°, and measurement of the steadiness under isometric contraction and not isokinetic – limit one's ability to make definitive conclusions about the efficacy of the program.

In contrast to local EMS, WBEMS focuses on the stimulation of large segments of muscle during contractions.[133] Previous studies have shown that WBEMS increases resting metabolic rate[134] and energy expenditure.[133] Accordingly, WBEMS has been proposed as a potentially beneficial modality for improving energy balance among overweight and obese individuals.[134] Two studies have also reported significant strength gains between 25–38% in response to WBEMS.[135,136] However, the majority of studies have reported relatively small increases in maximum muscle strength (≤ 15%) following WBEMS. These changes are rather small when compared to common changes that are observed as a result of standard resistance training regimens. Furthermore, WBEMS has not demonstrated the ability to induce meaningful changes in lean muscle mass,[129] suggesting that neural adaptations are likely to explain the mechanism for any increase in strength and/or power.

Despite widespread use of local or whole-body EMS in clinical and athletic populations; the relative lack of well-controlled studies in seniors limits its present utility as a means to maintain physical function and prevent disability. Furthermore, the available literature has not clearly demonstrated any advantage of this method over traditional muscle strengthening techniques. Still, there is at least some evidence to suggest older individuals with physiological limitations or who are unwilling/unable to perform vigorous resistance training programs may benefit from EMS. In summary, continued investigation of this area

is needed to better understand its potential utility as a clinical modality for maintaining physical function among older adults.

4.2 Blood flow restriction exercise (KAATSU)

As reviewed recently, exercise performed while blood flow is mildly restricted holds potential as an alternative to high-intensity resistance training.[137] Blood flow-restricted exercise, also known as KAATSU, involves performing low-intensity resistance exercise while externally-applied compression mildly restricts blood flow to the active skeletal muscle. Because KAATSU training eases joint stress by avoiding high-intensity loads, it has been proposed as a potentially efficacious method of improving muscle strength among persons for which high-intensity resistance training is medically contraindicated or infeasible.[137–139]

The concept of exercising while restricting blood flow has been around for nearly 40-years, and was popularized in Japan in the mid-1980's. Literally translated, KAATSU means "muscle strength testing with the addition of pressure." This paradigm utilizes a relatively simple approach that generally involves inflating a narrow compression cuff (11–15 cm wide) around an appendicular limb proximal to the muscle group being trained. The compressive pressure varies between studies, but typically the cuff is inflated to a pressure greater than brachial systolic pressure. Notably, the compressive pressure experienced at the artery is less than the tourniquet pressure due to soft tissue compliance.[140] As such, cuff pressure occludes venous return and causes arterial blood flow to become turbulent and thereby reducing blood velocity distal to the cuff.

Mounting evidence demonstrates that KAATSU training serves as a potent stimulus for increasing skeletal muscle mass and strength[141–143] – as well as muscular endurance.[144,145] This observation that exercise performed with low mechanical loads seemingly opposes traditional beliefs regarding processes of muscle adaptation and as such has been met with some interest by researchers.[146] To this end, several recent studies have attempted to identify the molecular mechanisms regulating KAATSU-induced increases in muscle function. These studies have demonstrated that KAATSU stimulates a number of beneficial adaptations – including regulating mechanisms that govern myofibrillar protein balance,[147–149] vascular supply,[143,144,150,151] and neuromuscular function.[149,152] As a result, this paradigm has been proposed as a potential therapeutic strategy to prevent sarcopenia and age-related functional decline.[139] However, although the available evidence has demonstrated the beneficial effects of chronic KAATSU training in young[143,150,153] and upper middle-aged[90] adults, to our knowledge no study has evaluated the relative efficacy of chronic KAATSU as a therapeutic strategy for preventing functional decline among older adults. Moreover, although recently published data indicate that older adults can safely perform acute bouts of KAATSU exercise,[154] questions remain regarding the safety of long-term KAATSU training for seniors as well as their willingness to adhere to the intervention. Accordingly, studies are needed to evaluate the feasibility of long-term KAATSU interventions for older adults.

5. Alternative Training Paradigms

Exercise guidelines for older adults generally recommend traditional forms of resistance and aerobic training.[155,156] However, some alternative forms of physical training may be more effective at addressing the specific age-related physical impairments that lead to functional decline. Indeed, skeletal muscle adaptations to resistance training are highly dependent on several programming variables such as load, volume, speed of contraction, and movement specificity. Though this point is widely recognized in fields which utilize exercise training to promote athletic performance, it seems to be less emphasized in the literature related to the prevention of disability among the elderly. Here we discuss several training regimens which capitalize on the understanding and manipulation of these programming variables and their potential application to improving function among older adults.

5.1 High-velocity (power) and eccentrically-biased training

Interventions manipulating either the speed or direction of muscle contraction during resistance exercise are among the most studied paradigms to optimize the efficacy of exercise for older adults. Two of the most commonly studied interventions of this type are (1) high-velocity resistance training, otherwise known as power training and (2) eccentrically-biased resistance training. Power training utilizes high speed muscle contractions, generally during the concentric phase of movement. The rationale for power training is that muscle power (the product of force and movement velocity) declines earlier and more rapidly in older adults than muscle strength.[157–159] Moreover, several studies have indicated that maximal muscle power is more closely associated with physical function than maximal strength.[160–163] A number of randomized trials have been conducted to compare power training to conventional resistance training. The cumulative results of these studies suggest that power training is more effective than conventional resistance training for enhancing muscle power[164–166] and has been shown to improve both muscle size[167] and maximum contraction velocity.[168] While power training has been shown to be effective for enhancing physical function, it remains unclear whether this effect does[11,165] or does not[164,169] exceed that of conventional resistance training.

Resistance training which highlights the use of eccentric, or lengthening, contractions has also received significant interest from scientists. Eccentric training is conducted using specialized equipment such as an isokinetic dynamometer[170,171] or by performing the concentric phase of movement bilaterally and the eccentric phase unilaterally.[172] Previous research has demonstrated that older adults' muscle strength is preserved to a greater extent during eccentric muscle contractions compared to concentric muscle contractions.[173,174] Therefore, eccentric contractions may allow the individual to train with greater relative intensity, which is crucial for eliciting beneficial muscular adaptation.[175] It has also been proposed that eccentric contractions require a different neural activation strategy compared to concentric contractions. For instance, cortical activation measured with electroencephalography during eccentric contractions shows earlier onset, higher magnitude and larger area of activation than during concentric contractions.[176,177] Training with eccentric contractions has also been reported to induce a larger cross-transfer of strength improvements to the untrained limb,[178,179] indicating greater involvement of bilateral motor

control mechanisms. Accordingly, eccentric contraction may be a more potent stimulus for eliciting beneficial neural adaptation. The potential advantages of eccentric resistance training might be particularly important when initiating a resistance training intervention in older adults with poor muscle strength.[180]

Consistent with the advantages suggested above, reported benefits of eccentric training include improvements in strength[171,178,181,182], muscle size,[181–184] neuromuscular activation,[171] and cross-transfer of strength improvements.[171,178,179] Cumulatively, there is considerable evidence that muscular and neural adaptation with eccentric training may exceed that of concentric training in healthy adults. However, it is important to note that studies do exist which have reported little to no additional benefit of eccentric resistance training over conventional training.[170,172] Furthermore, the benefits of eccentric training are often very specific to the trained contraction velocity and mode. Accordingly, additional research is needed to optimize the use of eccentric resistance training for older adults, particularly in the context of promoting transfer of improvements to physical function.

5.2 Task-Specific Exercise

A wealth of previous research indicates that traditional exercise modalities enhance numerous aspects of physical performance. However, the extent to which these benefits transfer to improving the ability to perform ADLs has been questioned.[164,185] Issues surrounding the transfer of specific exercise adaptations to the performance of ADLs may stem at least partially from a lack of training specificity during these interventions. The well-established principle of training specificity dictates that the largest improvements in task performance stem from training paradigms that closely simulate the task.[186] Accordingly, task-specific exercise (TSE) training, also known as functional exercise training, was designed to address the task specificity limitation of traditional exercise programs and improve the performance of ADLs related to physical disability. These programs involve practicing functional tasks, such as chair rises, stair climbing, and walking under different challenging conditions.[187–189] As such, TSE training offers older adults the opportunity to improve basic components of physical function (e.g., muscle strength and balance) within an ecologically valid context that may also enhance relevant cognitive and perceptual factors. Limited evidence suggests TSE training may also produce neural plastic changes that could underlie functional improvements.[190]

Previously, de Vreede at al.[191] demonstrated that both TSE and resistance training significantly improved ADL performance among community-dwelling older women. Though not statistically significant, the TSE group scored better on the Assessment of Daily Activities Performance scale, with a mean change of 7.5 units, compared to the resistance training group's mean change score of 2.8 units. Both programs also led to gains in knee extensor strength. In a separate study, these authors reported that neither 12 weeks of TSE nor resistance training led to changes in self-reported health related quality of life.[192] Recently, Manini et al. reported that TSE significantly reduced performance time of ADLs, but did not lead to muscle adaptations, whereas resistance training increased muscle strength, but had no impact on ADL performance time.

Other studies have combined TSE with resistance training by requiring participants to wear a weighted vest or carry progressively heavier loads while performing standard resistance exercises.[188,193–195] Notably, while the exercises in these interventions specifically trained muscles used in mobility tasks, these exercises did not simulate ADLs as closely as standard TSE interventions. Still, in a small sample of older women with mobility impairments, this type of TSE plus resistance training enhanced leg power and improved chair stand time, compared to a slow-velocity, low-resistance exercise program.[193] Both TSE and low resistance training interventions significantly improved SPPB scores. However, studies with larger sample sizes have indicated that the benefits derived from these TSE programs were not meaningfully different than those produced by a National Institute on Aging (NIA) recommended exercise program[188] or traditional resistance training intervention.[196] Similar combination TSE interventions have also been applied in long-term residential care settings, though with little success.[194,195]

Taken together, the available evidence tentatively supports the notion of using TSE to improve physical function and ADL performance. However, numerous methodological limitations within the extant literature preclude drawing firm conclusions regarding the efficacy of TSE. Future research using larger, more diverse samples is required to systematically assess TSE interventions, particularly those comprised of exercises that closely simulate ADLs. Additionally, a well-designed RCT is needed to determine whether TSE can provide older adults with additional functional benefits than currently recommended exercise programs.

5.3 Dual-task training

In addition to physical factors, cognition plays an important role in the performance of functional tasks.[197,198] Optimal task performance requires the capability to attend to and process information about task objectives and external conditions. For example, walking in a crowded environment or walking while maintaining a conversation may place a high demand on information processing resources. This can be a challenge for many seniors as available cognitive resources typically decline with age.[199,200] As a result, “dual-tasking” paradigms have been used in research to assess an individual’s capability to process multiple sources of motor and/or cognitive information simultaneously. Dual-tasking has also been used in exercise interventions to target the mechanisms of impaired information-processing and induce gains in functional task performance.

Recently, several randomized controlled trials have indicated a beneficial effect of dual-task training on physical function in older adults. For instance, Shigematsu et al. [201] randomized 68 older adults to a 12-week “square-stepping” training protocol or a standard walking protocol. Square stepping required participants to walk over a course that was divided into a grid of squares and move across the grid using increasingly complex patterns of foot placement during stepping. Following the interventions, the group trained with square stepping exhibited larger gains in leg power, balance, agility and reaction time compared to the walking group. Another study of 23 older adults with balance impairments compared balance and gait performance following 4 weeks of either single or dual-task training.[202] These findings indicated that both training regimens improved walking speed, but only dual-

tasking improved walking speed when the test was accompanied by a simultaneous cognitive challenge. Moreover, Pichierri et al. [203] recently compared the utility of a standard strength and balance intervention to cognitive-motor training using a dance video game. In a sample of 30 older adults, the group that trained with the dance video game demonstrated better performance on an assessment of fast dual-task walking, but the groups did not differ on tasks of foot placement accuracy or falls efficacy.

Cumulatively, there is enticing evidence to suggest a benefit of dual-task training compared to standard training regimens. However, the wide variety of tasks used for training and assessment – as well as the small sample sizes utilized in the available studies – make it very difficult to estimate the magnitude and generalizability of the effect. Future research should be directed toward defining the parameters of dual-task training that are most crucial for inducing gains in function. Such studies should also provide further evidence regarding the level(s) of cognitive reserve necessary to benefit from such interventions.

6. Environmental Modification

Environmental limitations often represent a significant barrier to regular engagement in exercise by older adults. For example, older adults who live in rural or low income areas may have difficulty accessing recreational facilities or other locations in which they can be physically active. Additionally, many neighborhoods may not have adequate sidewalks, bike paths, or other open areas that would encourage physical activity. Although studies examining the effects of the environment on physical activity in older adults are limited, available evidence suggests that making the surrounding environment more conducive to physical activity would increase activity levels in all segments of the population.[204–206]

Greater distance to recreational facilities may represent a barrier to exercise specifically for older adults due to potential financial and safety concerns related to driving long distances. Difficulties in performing regular ADLs may also be a barrier for seniors to regularly engage in formal training regimens.[207] Given the potential benefits of exercise training regimens for enhancing physical function in older adults, a key question is how to improve adherence to exercise regimens in this population. Various strategies that have been examined to enhance exercise adherence, primarily in young and middle-age adults, include home-based exercise, the provision of home exercise equipment, the use of short bouts of exercise, and monetary incentives for exercise.[208] Of these strategies, home-based exercise regimens have received the most consistent support for enhancing long-term exercise adherence.[209] In contrast to supervised group exercise sessions, home-based exercise offers a greater degree of flexibility and fewer obstacles. The benefits of home exercise may also be enhanced by providing participants with exercise equipment and by allowing them to exercise in brief bouts. For example, Jakicic et al.[210] reported that participants who received home exercise equipment had significantly higher levels of long-term exercise adherence than participants without exercise equipment. Additional research is now needed to further examine the types of home-based training programs that can produce high levels of adherence and functional benefits among older adults.

Conclusion

In recent years, numerous studies have indicated a wide variety of benefits of exercise to the physical health of older adults. Indeed, exercise is increasingly being considered the standard of care for preventing disablement among seniors. Still, accumulating evidence indicates that a "one-size fits all" approach isinsufficient to fully meet the needs of the heterogeneous older adult population. Accordingly, like other aspects of medicine, exercise regimens should be individually tailored to ensure the highest level of benefit for all individuals.[211,212] The present review summarizes a variety of approaches which have been studied in attempting to optimize the beneficial effects of exercise on the physical function of older adults (Figure 2). Several of these interventions appear to hold promise for enhancing the benefits of exercise for at least some older adults. However, insufficient evidence regarding the efficacy of many of these interventions precludes drawing firm conclusions and making clinical practice recommendations. As such, future research in this area is needed using well-controlled, larger-scale studies which can make an impact on clinical practice. Such research is critical to the development of clinical practice recommendations which will have a lasting impact in maintaining the health and independence of the rapidly increasing number of older adults.

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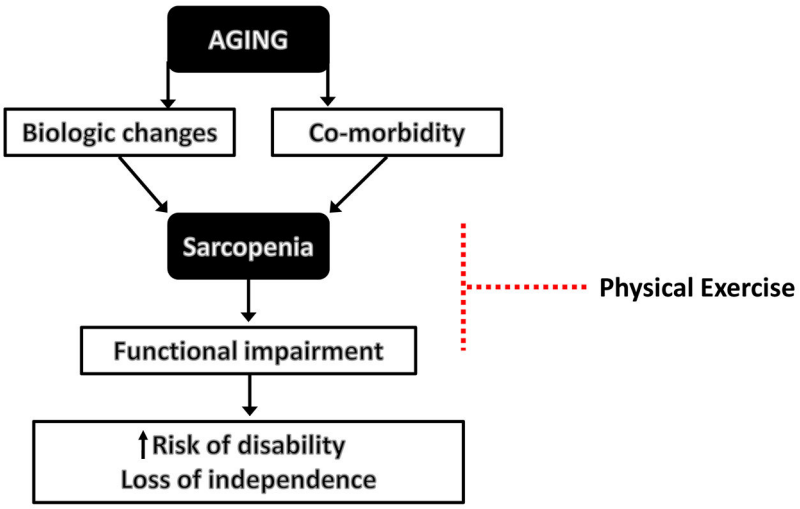

Figure 1.

Simplified schematic of the development of physical disability among older adults and the potential of exercise to slow or prevent this development. The use of a dashed line highlights the variability of responsiveness and that standard exercise programs may be insufficient to prevent disability among several sub-groups of seniors.

Figure 2.

Summary diagram depicting potential methods to optimize functional responses of older adults to exercise. Specific examples of potential interventions are discussed within the text.