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What is dynapenia?

Brian C. Clark, Ph.D.[a,*] and **Todd M. Manini, Ph.D.**[b]

[a]Ohio Musculoskeletal and Neurological Institute (OMNI) and Department of Biomedical Sciences, Ohio University, Athens, Ohio, USA

[b]Institute on Aging and Department of Aging and Geriatric Research, University of Florida, Gainesville, Florida, USA

Abstract

Dynapenia (pronounced *dahy-nuh-pē-nē-a*, Greek translation for poverty of strength, power, or force) is the age-associated loss of muscle strength that is not caused by neurologic or muscular diseases. Dynapenia predisposes older adults to an increased risk for functional limitations and mortality. For the past several decades, the literature has largely focused on muscle size as the primary cause of dynapenia; however, recent findings have clearly demonstrated that muscle size plays a relatively minor role. Conversely, subclinical deficits in the structure and function of the nervous system and/or impairments in the intrinsic force-generating properties of skeletal muscle are potential antecedents to dynapenia. This review highlights in the contributors to dynapenia and the etiology and risk factors that predispose individuals to dynapenia. In addition, we address the role of nutrition in the muscular and neurologic systems for the preservation of muscle strength throughout the life span.

Keywords

Aging; Strength; Weakness; Function; Muscle; Disability; Sarcopenia; Dynapenia

What is dynapenia?

A staggering 16% to 18% of women and 8% to 10% of men in the United States older than 65 y cannot lift 10 lbs. or stoop/kneel down [1]. Physical functioning tasks of this nature are undoubtedly closely linked to physiologic capabilities, such as muscle strength and power production, and low muscle strength is well known to place older adults at an increased risk of mobility limitations [2-8] and mortality [9-12]. Accordingly, the preservation of muscle strength and power with advancing age is of high clinical significance. It was once thought that the well-characterized age-related atrophy of muscle was to blame for poor muscle strength. However, recent longitudinal and intervention-based studies have clearly demonstrated that muscle atrophy is a relatively small contributor to the loss of muscle strength [13-16]. Similarly, longitudinal studies delivering exogenous supplementation of androgens or growth factors have yielded an increase in muscle mass but only marginally improved muscle performance [17,18]. However, despite findings of this natured—and similar findings from more than 30 y ago [19]— the preponderance of scientific investigations have continued to focus primarily on determinates of skeletal muscle size. In 2008 we proposed the term *dynapenia* to define the age-related loss of muscle strength and power [20]. *Dyna* refers to “power, strength, or force” and penia refers to “poverty.” We

*Corresponding author. Tel.: +740-593-2354. clarkb2@ohio.edu (B. C. Clark).

should note that Morley et al. [21] recently used the term *kratopenia* to characterize the "loss of force" and *dynapenia* to characterize the "loss of power." In the context of this review, we refer to dynapenia within the context of our original definition, which encompasses the broader aspects of skeletal muscle force performance and includes strength (i.e., maximal voluntary force) and/or mechanical power (a product of force times velocity), which are commonly measured using dynamometry equipment (e.g., isometric strength, isokinetic power, etc.). In the following paragraphs, we provide details on the causes and consequences of dynapenia.

What are the consequences of dynapenia?

The consequences of dynapenia are staggering; it increases the risk for physical disability [22,23], poor physical performance [2-8], and even death [9-12]. For example, we recently conducted an informal meta-analysis examining the relative risk between low levels of muscle strength and poor physical performance and/or physical disability. We found that in the vast majority of studies (90%), a significant association was noted, with the unweighted average of the relative risks being 2.2 (Fig. 1) [24]. As an aside, only 35% of the studies found significant associations with sarcopenia. We should note that there are limitations in presenting unweighted average relative risks [25]; however, the findings suggest that dynapenia is an important prognostic indicator of functional impairments in elders. With regard to the impact of dynapenia on mortality, Newman et al. [9] observed that grip and knee extensor muscle strengths were strongly related to mortality (even after accounting for muscle area and regional lean mass). Specifically for women, they observed crude hazard ratios of 1.84 for grip strength and 1.65 for knee extensor strength. For men, they observed crude hazard ratios of 1.36 for grip strength and 1.51 for knee extensor strength. More recently, Xue et al. [10] reported in a longitudinal study of 436 women that faster rates of decreases in grip and hip flexor strengths independently predicted mortality after accounting for potential confounders. The hazard ratios were 1.33 and 2.62 for the rates of decrease in grip and hip strengths, respectively. Collectively, these findings provide convincing data that dynapenia in older adults have serious negative consequences as it relates to physical disability, physical function, and mortality.

What are the contributors to dynapenia?

It was originally thought that the loss of skeletal muscle mass (sarcopenia) largely explained the dynapenia commonly observed in older adults [26]; however, recent longitudinal data have suggested that other physiologic factors—independent of tissue size—play an important and likely larger role in determining who will develop muscle weakness [15]. Specifically, data from the Health, Aging and Body Composition study—a large prospective cohort of older adults—have indicated that the decrease in muscle strength is significantly more rapid than the concomitant loss of muscle mass, and that the change in quadriceps muscle area explains only ~6% to 8% of the between-subject variability in the change in knee extensor muscle strength [15]. Moreover, maintaining or gaining muscle mass does not prevent aging-related decreases in muscle strength [15] (Fig. 2). Accordingly, these findings indicate that the loss of muscle strength in older adults is weakly associated with the loss of lean body mass. Other findings using experimental disuse models of muscle weakness (e.g., bedrest) also have suggested that the relative contribution of muscle atrophy to weakness is modest [13,14,16]. For example, we have reported that the loss of muscle mass after 4 wk of leg muscle disuse (i.e., unilateral lower limb suspension, where one leg is unweighted by having young, healthy study participants ambulate on crutches) explains less than 10% of the associated loss of muscle strength [13,14]. Rather, our experimental disuse findings largely indicated that changes in neurologic function and/or the intrinsic force-generating

properties of skeletal muscle contribute to muscle weakness and motor dysfunction [13,14,27-30]. Later we discuss the potential physiologic contributors to dynapenia.

In brief, the contributors to dynapenia can be compartmentalized into two factors, i.e., 1) neurologic and 2) skeletal muscle properties, because it is well known that the output from these sources controls muscle force production [20,27,31]. For example, it is plausible that the nervous system's ability to fully activate skeletal muscle voluntarily is impaired in dynapenic individuals, with this deficit in voluntary (central nervous system) activation caused by potential changes, such as a decreased excitatory drive, to the lower motor neurons and/or decreases in α-motor neuron excitability, which could result in suboptimal motor unit discharge rates [32]. In addition, dynapenic individuals could have fewer functioning motor units, which would theoretically affect muscle strength once a critical threshold is reached, particularly if collateral reinnervation does not occur or is incomplete. This is a logical pathway because it is clear that older adults possess fewer motor units compared with young adults [33,34]. Similarly, it is plausible that the muscle system's ability to optimally produce force is impaired in dynapenic individuals, with this deficit in the intrinsic force-generating capacity of muscle (force/unit area) caused by potential changes in the excitation–contraction coupling process [35,36]. Figure 3 provides a conceptual model for how impairments in the nervous and muscle systems can contribute to dynapenia and subsequently lead to functional limitations, which subsequently place older adults at risk of physical disability. Later we describe the potential physiologic factors leading to dynapenia.

Can older adults fully activate their skeletal muscles during a muscle contraction?

There is no question that impairments in the nervous system's ability—or lack thereof—to fully activate skeletal muscle could, theoretically, be an explanatory contributor to dynapenia. Indeed, there is evidence to suggest that aging results in impaired agonist activation and/or increased antagonistic coactivation [37]; however, age-related differences in voluntary activation appear to vary between muscle groups and likely varies between subclasses of older adults (e.g., healthy versus physically disabled). Before more fully discussing the effects of aging on voluntary activation, we provide a brief overview of the assessment of voluntary activation [38,39]. A voluntary effort, or a voluntary contraction of a muscle, consists of the recruitment of motor neurons and, hence, muscle fibers by an increased descending drive. Hence, with an increased force of contraction, there is an increased activation of neurons in the primary motor cortex with increased firing of corticospinal neurons [40]. An increased descending drive recruits larger numbers of motor neurons in the spinal cord. Concomitantly, force summates more effectively because the central nervous system varies the rate of neuronal firing, thereby generating increased force at higher frequencies. This is known as *rate modulation* or *rate coding*. Nevertheless, each motor neuron innervates a number of muscle fibers that fire one-to-one with the motor neuron. Together, these comprise a motor unit. When a motor unit fires sufficiently fast, its muscle fibers produce a fused contraction. Although there are many influences on motor neurons during voluntary contractions, such as excitatory and inhibitory sensory feedback, and alterations in motor neuron properties that may make them more or less responsive to synaptic input [41], the descending drive from the motor cortex is the major determinant of the timing and strength of voluntary contractions.

Voluntary activation is commonly assessed using the interpolated twitch method or a derivative thereof (e.g., central activation ratio) [38,42]. Here, the motor nerve to the muscle, or the muscle itself, is electrically stimulated during a voluntary effort. During maximal voluntary efforts, any increment in force evoked by a stimulus indicates that

voluntary activation is less than 100%. That is, some motor units are not recruited or are not firing fast enough to produce fused contractions [43]. The extra force evoked by stimulation during contraction can be quantified by comparison with the force produced by the whole muscle. Thus, voluntary activation represents the proportion of maximal possible muscle force that is produced during a voluntary contraction. Measurement of voluntary activation does not quantify the descending drive reaching the motor neurons or whether motor neuron firing rates are maximal, and it does not take into account the source of the drive to the motor neurons. However, mechanisms in the cortex, spinal cord, and muscle can influence voluntary activation [38].

There are equivocal reports in the literature on whether advancing age decreases voluntary activation capacity [44-63]. A synthesis of the literature, however, does provide some insight into potential explanations of these equivocal reports. Specifically, several studies examining the effect of age on voluntary isometric activation of the knee extensors [50,60] and the elbow flexors [44,51,52] have suggested that older adults, particularly those older than 70 to 75 y, exhibit a decrease in voluntary activation, whereas investigations on the age-related changes in the voluntary activation of the dorsiflexors yielded null findings [47,48,53,57,59,63]. Because of the functional differences between these muscles and the differences in their physiologic profiles (e.g., motor unit innervations and fiber type characteristics), these muscle-group specific effects are not overly surprising, especially when one considers that differences in the activation of different muscle groups have been reported in young subjects [42]. We should note there are several studies indicating that older adults have a meaningful level of impairment in voluntary activation. The impairments found in central activation are large enough to explain a large portion of observed muscle weakness in a given individual, such as inactivation on the level of ~ 15% or more [50,52,60]. One study that deserves particular attention is by Harridge et al. [50], which entails, to our knowledge, the oldest known cohort of individuals to date to undergo these types of assessments (n = 11, age range 85–97 y). In this study, all older adults required some degree of assistance with everyday activities, and—interestingly—all subjects showed evidence of incomplete voluntary activation during a maximal contraction, with activation ranging from 69% to 93% (mean 81 ± 7%). This finding suggests that deficits in voluntary activation can contribute to a significant portion of the muscle weakness observed in the very old.

What are the potential neurophysiologic mechanisms of dynapenia?

As stated previously, physiologic factors in the cortex, spinal cord, and muscle can influence voluntary activation. The neurons in the premotor and primary motor cortex form a complex network of glutamatergic interneurons, afferent projections, and pyramidal neurons that project to the striatum and spinal cord, among other areas of the central nervous system. Although it is often widely assumed that there is a progressive decay in the number of primary motor cortex (M1) neurons in normal aging, the available evidence suggests there is no such consequence with aging [64,65]. However, there are substantial morphometric changes in the motor cortex that do occur in with normal aging. For example, cadaveric dissections have suggested that individuals older than 65 y exhibit a staggering 43% volumetric decrease in the premotor cortex neuron cell body size compared with younger adults [64], and these observations have more recently been corroborated in living humans using high-resolution magnetic resonance imaging [66]. Furthermore, there is also evidence to suggest that age-related differences exist in the mass of white matter and of myelinated nerve fiber length, with individuals losing ~45% of the total length of the myelinated fibers, mostly in the smallest white matter nerve fibers [67]. Also, evidence from cross-sectional studies further has suggested that aging disrupts the integrity of the white matter [68].

Functionally, it appears that these changes from aging affect the connectivity of the cortex with itself and the rest of the central nervous system.

Aging also affects motor cortical properties at the systems level. Specifically, aging has been shown to result in decreased cortical excitability [69-72], increased activation in areas of sensorimotor processing and integration [73-75], and decreased cortical plasticity [76,77]. For example, using transcranial magnetic stimulation—a non-invasive technique that provides insight into human motor cortex excitability—we recently reported that older adults exhibit more intracortical inhibition and less intracortical facilitation compared with young adults [70], which is consistent with our observation of disuse-induced muscle weakness being associated with increases in intracortical inhibition [28,30]. In addition, the human motor cortex displays an age-dependent decrease in cortical plasticity [76,77], where the paired-associative electrical stimulation of the median nerve that increases the motor evoked potential amplitude in young and middle-aged adults is impaired in older adults [76]. Collectively, these findings suggest that aging results in decreased motor cortical excitability and cortical plasticity, which may contribute to age-related decreases in muscle performance.

In addition to these potential cortical mediators of dynapenia, age-related changes in spinal neurophysiologic properties could contribute to dynapenia because motor units demonstrate numerous age-related adaptations, including changes in morphology, behavior, and electrophysiology. With regard to changes in morphology, advancing age is thought to result in a smaller motor unit number and an increased number of fibers per motor unit (increased innervation ratio) because of the compensatory collateral sprouting by surviving neurons [34, 78-80]. Aging has also been shown to result in changes in spinal excitability. For example, Kido et al. [81] reported that the soleus H-reflex (a global measurement of spinal excitability) decreased gradually with age. Others have also observed that heteronymous facilitation [82] and oligosynaptic reflexes [83] decrease with age, which provides collective evidence that there is a general decrease in the excitability of spinal reflexes with age. The end result of the morphologic and physiologic adaptations in motor units with aging is alterations in the behavioral discharge properties of motor units. For instance, older adults have been reported to exhibit maximal motor unit firing rates that are ~35% to 40% lower than in young adults [84]. These lower firing rates appear to be largely inter-related to the longer twitch contraction durations in older muscle, which further illustrates the critical integrative control processes involved between the nervous and muscle systems as they relates to overall neuromuscular function. More recent evidence has suggested that more subtle age-related differences exist in motor unit behavior. Specifically, older adults have been reported to exhibit a greater variability in motor unit discharge rates that appears to largely influence their ability to maintain steady forces [85], and the occurrence of motor unit doublet discharges is lower in older adults [86]. Collectively, these changes in motor unit discharge properties likely contribute to the decreased functional properties of aged skeletal muscle.

What are the potential muscular mechanisms of dynapenia?

Muscle atrophy undoubtedly occurs with advancing age. More Specifically, recent longitudinal data have indicated that, on average, older men lose approximately 1% of their thigh muscle area per year and older women lose approximately 0.65% of their thigh muscle area per year [15]. With this stated—as illustrated in Figure 2—it should be noted that there is a large between-subject variability in the degree of atrophy observed with aging, and some older adults appear to exhibit no or nominal losses in muscle mass [15]. Several studies have indicated that the atrophy is primarily caused by a loss of fibers, with no predominant effect on any fiber type, and to a lesser extent by a decrease in fiber size—predominantly type II

fibers [87,88]. There are many interacting factors leading to muscle wasting in older adults, and they often present themselves concurrently. Changes in muscle protein metabolism have been proposed as an explanatory factor in muscle wasting in older adults, because the balance between protein synthesis and degradation is largely responsible for the maintenance of lean mass. However, recent findings have suggested that basal muscle protein synthesis rates do not differ between young and old adults [89-94], and it is generally accepted that the difference in fasted rates of muscle protein synthesis or breakdown are not altered in healthy older adults [95]. Current hypotheses related to causative factors affecting muscle protein turnover surround the concept of older adults being resistant to anabolic stimuli, such as that associated with feeding, insulin, or physical activity. For example, although the ingestion or infusion of large quantities of amino acids/protein (~30–40 g) yield similar increases in muscle protein synthesis in young and older individuals [96-100], recent studies have indicated that older adults exhibit a decreased accretion of muscle proteins after the ingestion of smaller amounts of essential amino acids (6–15 g) [90,91]. Similarly, several recent studies have reported a blunted muscle protein synthesis response after an acute bout of resistance exercise in older subjects [101-103]. So, although muscle atrophy and changes in muscle protein metabolism undoubtedly occur with aging, as stated earlier, the relative contribution of the loss of muscle size associated with advancing age toward the observed muscle weakness is substantially less than originally assumed. In the following paragraphs, we summarize the other potential muscular mechanisms of dynapenia.

In addition to muscle size and anatomic structure, aged muscle appears to differ in other compositional manners. For instance, over the past decade, numerous studies have reported that aging increases the adipocyte content between muscle groups (intermuscular adipose tissue) and between muscle fascicles (intramuscular adipose tissue) [15,104,105]. The earliest of these studies suggested that greater muscle fat content is associated with decreased muscle strength [105], suggesting a potential mechanistic link between increases in fat infiltration in muscle and muscle weakness. Indeed, cytokine production from adipose tissue has been linked to decreased muscle force production [106,107], thus providing a theoretical basis to this assertion. However, more recent longitudinal data have failed to observe a direct relation between increased levels of intermuscular adipose tissue and strength loss with age [15]. Other compositional changes have also been speculated to potentially alter the intrinsic force-generating properties of aged skeletal muscle, such as changes in the ratio of myosin to actin [108], the functional interaction of actin and myosin proteins [109-111], the expression of the thin filament regulatory proteins troponin and tropomyosin [112], and/or the expression of cytoskeletal proteins [113]. However, currently little attention has been paid to these potential contributors as they relates to dynapenia, and further work is needed to better delineate their relative contributions.

A likely muscular contributor to dynapenia is impairment in the excitation–contraction coupling processes, which are series of biophysical events involved in converting the electrical signal for muscle activation into contractile force. Theoretically speaking, the disruption of any of the events in the excitation–contraction coupling process could result in the suboptimal activation of muscle, thus decreasing muscle quality (force per unit tissue area), and contribute to dynapenia. In particular, impairments in calcium (Ca^{2+}) release from the sarcoplasmic reticulum have been suggested to explain the deficits of muscle quality (the intrinsic force-generating capacity of skeletal muscle relative to its tissue size) in aged muscle [113-123]. The effects of aging on the principal proteins involved in voltage-induced Ca^{2+} release (e.g., ryanodine Y receptors and dihydropyridine receptors) have received the most scientific attention. These studies have indicated that older mammalian skeletal muscle exhibits decreases in the dihydropyridine receptor, namely the α-1s subunit, thus disrupting the voltage-induced Ca^{2+} release process [118-120]. We should also note that it has recently

been suggested that sarcoplasmic reticulum Ca^{2+} release impairment can occur independent of dihydropyridine receptor function [113]. Specifically, Russ et al. [113] observed a decreased protein–protein interaction between the ryanodine Y receptor and FKBP older rat muscle, which they suggested may result in decreased muscle quality. It should be noted that the role for sarcoplasmic reticulum-related proteins that are not directly involved in Ca^{2+} release has begun to be investigated recently (e.g., junctophilin and mitsugumin 29). Some of these proteins, which are associated with the triadic junctions between the t-tubules and terminal cisternae, appear to decrease with age [122,123] and may negatively affect the structure–function relation of the sarcoplasmic reticulum and t-tubules.

What are future directions for research in dynapenia?

The obvious long-term goal of scientific investigations within this area is to develop effective interventions to prevent and treat dynapenia, which ultimately should lower the rates of physical limitations in eldery adults. However, to achieve this goal, we believe that several critical issues need to be urgently addressed. First, an objective definition of dynapenia that is agreed on by a consensus panel is needed. A definition would expand clinical research by setting a universal criterion that can be compared across clinical centers. Such consensus definitions are immensely helpful in providing clear goals for experimental interventions (nutritional or otherwise) and success in combating disease. There have been some attempts to generate a definition for sarcopenia (not dynapenia). In one attempt, the European Working Group on Sarcopenia in Older People treated sarcopenia as a syndrome by including gait speed and grip strength in the operational definition. According to their decision algorithm, all adults older than 65 y should be assessed for gait speed. It is then recommended that individuals with a gait speed slower than 0.80 m/s be tested for appendicular or total muscle mass that is used to diagnose sarcopenia. Older adults without gait speed impairments (>0.80 m/s) would perform a grip strength assessment. Individuals with low grip strength are then referred for measurement of appendicular or total muscle mass to diagnose sarcopenia. The algorithm certainly has some strong points—namely feasibility, because gait speed and grip strength testing could easily be conducted at small clinics. However, the cutpoints proposed for low muscle mass have not resulted in consistently significant associations with health outcomes [124, 125], misclassifies obese older adults [125], and has a marginal discriminative ability in identifying older adults at risk of disability (area under the receiver operator curve ~0.70) [126]. The sarcopenic syndrome approach opens a difficult pathway for treatment because each component has a complex etiology that likely requires different intervention and treatment strategies. Such complexity also makes it difficult to target “at-risk” individuals. A new approach proposed by Morley et al. [21] defines sarcopenia as “low muscle mass with limited mobility.” The definition uses sarcopenia as it was originally intended (>2 SD loss in muscle mass compared with 20- to 30-y-olds) but adds that individuals with a gait speed slower than 1.0 m/s are those who should be targeted for clinical trials. This approach does not include muscular strength as a component and as such stays true to the original definition of sarcopenia. A consensus operational definition for dynapenia has not been developed, but we previously suggested a decision algorithm to initiate discussions along these lines [24]. Specifically, we proposed that adults older than 60 y undergo a brief screening for major disease risk factors. Those with low risk factors conduct a grip strength test, which is known to have a high specificity for identifying those not at risk of dynapenia. Those who screen for a large number of risk factors or test positive for low grip strength then undergo a knee extension strength test that is used to determine if an individual is dynapenic. Unfortunately, the data to test the validity of the detection algorithm are not yet available, although the data to test other algorithms are not available either. Today, we are at a crossroads on how to best define and characterize sarcopenia and dynapenia, which has resulted in some confusion in the literature and among experts in the field. Although this was not intended per se, we

believe these definitions and characterizations need to be simplified to promote the identification of target populations and the ability to conduct trials to determine if a given treatment strategy (e.g., therapeutic compound) is effective. One approach that we recently proposed surrounds developing a risk profile for low physical performance, which should likely include sarcopenia (as simply defined as the loss of, or low, muscle mass), dynapenia, and other potential contributors such as poor balance, depression, etc. The development of this risk profile would be similar to that seen in cardiovascular disease, which includes hypercholesterolemia, hypertension, and hyperglycemia as independent risk factors. Each factor has its own disease etiology and definition that can be targeted for interventions through changes in behavior, nutrition, and addition of pharmaceuticals. Such an approach could be developed for the loss in physical function—a multifactorial condition that includes sarcopenia and dynapenia and other risk factors yet to be fully determined.

Second, we need to identify biological contributors to dynapenia. That is, we need to better understand what is causing muscle weakness in older adults, and whether these specific contributors vary from person to person or clinical population to clinical population. Because studying the mechanisms of volitional force and movement control is difficult in animal studies—and because drawing cause-and-effect conclusions from human studies using a cross-sectional design is difficult—prospective, longitudinal cohort studies are urgently needed or, at a minimum, case–control studies that evaluate the potential biological contributors to dynapenia. Knowledge of this nature is needed to identify new therapeutic targets to alleviate dynapenia.

What role does nutrition play in dynapenia?

There is a substantial amount of literature examining the effects of dietary nutrients on the overall health of the nervous and muscular systems [127-129]; however, considerably less is known about the specific role of micronutrients on muscle strength. The emerging literature that does exist has largely focused on the effects of vitamins D and E, selenium, and carotenoids (α-carotene, β-carotene, β-cryptoxanthin, lutein, zeaxanthin, and lycopene). These findings have suggested that low levels of vitamin E [130-132], carotenoids [130,133], and selenium (that below a level that limits the synthesis of selenoproteins) [134,135] are associated with lower muscle strength. The mechanisms that dictate these associations are not completely understood, but are likely related to the control of oxidative stress that damages DNA, proteins, and lipids with aging. Interestingly, there is some evidence that carotenoid and selenium plasma concentrations are associated with inflammation (i.e., interleukin-6) [136], which is associated with lower levels of muscle strength [137-139]. Additional studies are needed to determine whether supplementation of carotenoids and selenium decrease inflammation to an extent that would affect muscle strength in elders.

In addition to the micronutrients mentioned earlier, there has been growing interest over the past 5 y on the impact of vitamin D on muscle (for review, please see Annweiler et al. [140]). Vitamin D receptors on muscle initiate the nuclear response leading to de novo protein synthesis and the activity of these receptors decreases with aging [141]. In addition, there is evidence that vitamin D receptors located on the hippocampus have a role in neuromuscular function [142]. However, the literature is conflicting on the association of vitamin D levels with muscle strength. For example, a recent review found that five observational studies demonstrated a relation between vitamin D and physical performance, whereas three studies found no such association [140]. In clinical trials, the evidence is even more contentious, with four studies finding a significant effect of vitamin D supplementation on muscle strength and three studies finding no effect [140]. More recently, Janssen et al. [143] found that supplementing the diet with cholecalciferol (400 IU/d + calcium 500 mg/d)

in women with low 25-hydroxyvitamin D levels did not change muscle strength compared with a group of individuals taking a placebo. This finding is consistent with a more recent study indicating that 150 000 IU of oral cholecalciferol delivered every 3 mo does not alter muscle strength [144]. Although more recent trials have not established a benefit of vitamin D supplementation on muscle strength, there remains controversy about the dosage, participant selection, level of plasma 25-hydroxyvitamin D needed to intervene, and the potential role of the parathyroid hormone [145-147]. As such, the effect of vitamin D on muscle strength requires further investigation.

Summary

Dynapenia is the age-associated loss of muscle strength. The biologic contributors to dynapenia are likely multifactorial and includes the nervous and muscle systems. However, the complex nature of dynapenia should not deter efforts that offer clear-cut definitions and knowledge about risk factors. We could learn much from other disciplines, where the complex etiology of the disease has not prevented an agreed-on consensus definition and clear risk factors that predispose individuals (e.g., hypertension, hypercholesterolemia, diabetes etc.). The clinical consequences of dynapenia are significant, because it increases the risk for functional limitations, disability, and mortality. Future work originating from many scientific disciplines, e.g., epidemiology and physiology, is required to provide the fundamental knowledge needed to eventually develop effective interventions to prevent and treat dynapenia.

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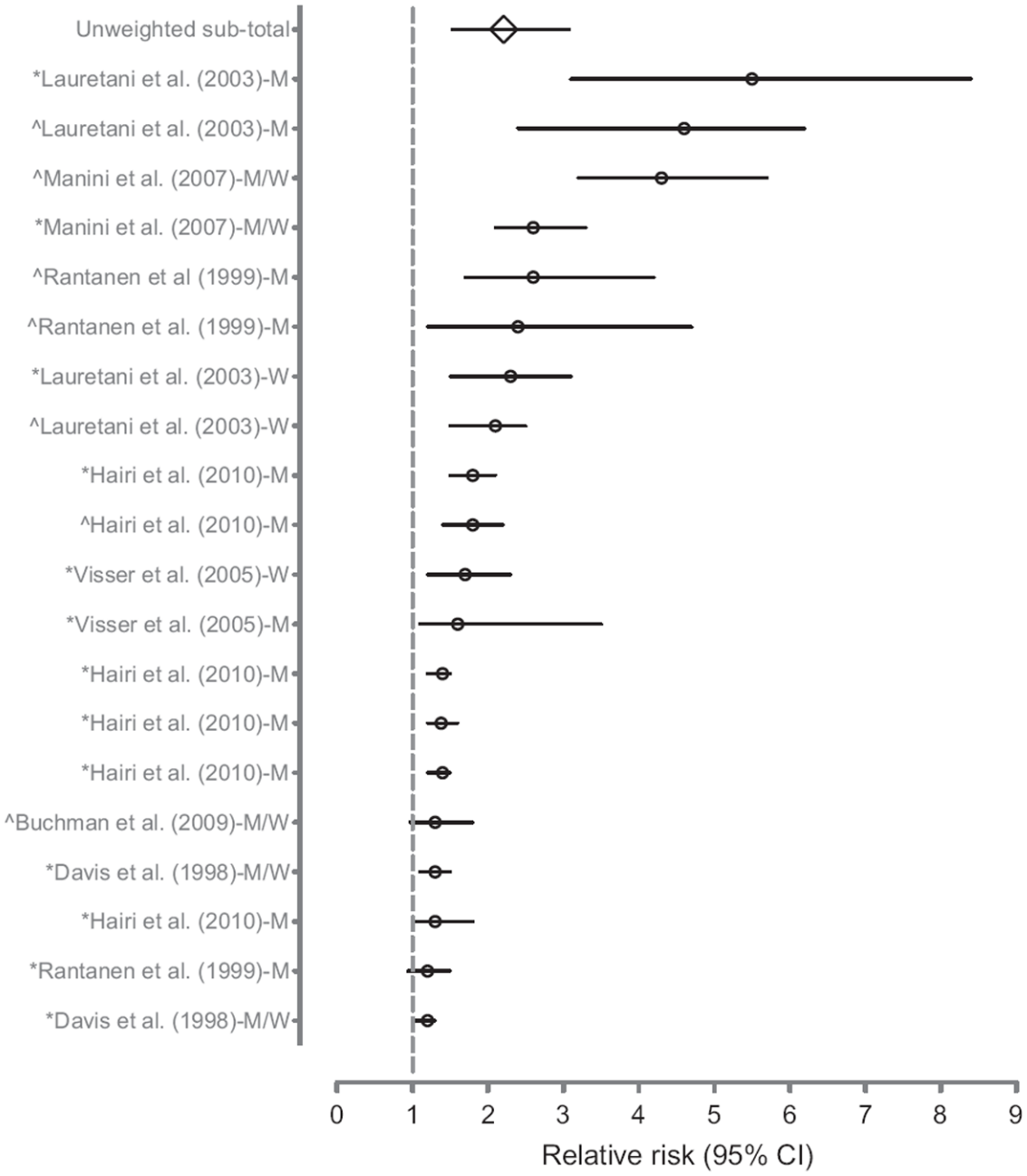

Fig. 1.

Relative risk of poor physical performance, functional limitation, or physical disability in older adults with dynapenia (low muscle strength). The counterfactuals are older adults with normal muscle strength or mass. Studies investigating multiple outcomes or expressing findings by sex are repeated. The author of each study is followed by whether the relative risk was estimated in men, women, or men and women and preceded by whether the outcome was a self-reported physical function/disability (*) or an observed physical performance (^). Figure modified from Manini and Clark. CI, confidence interval; M, men; W, women.

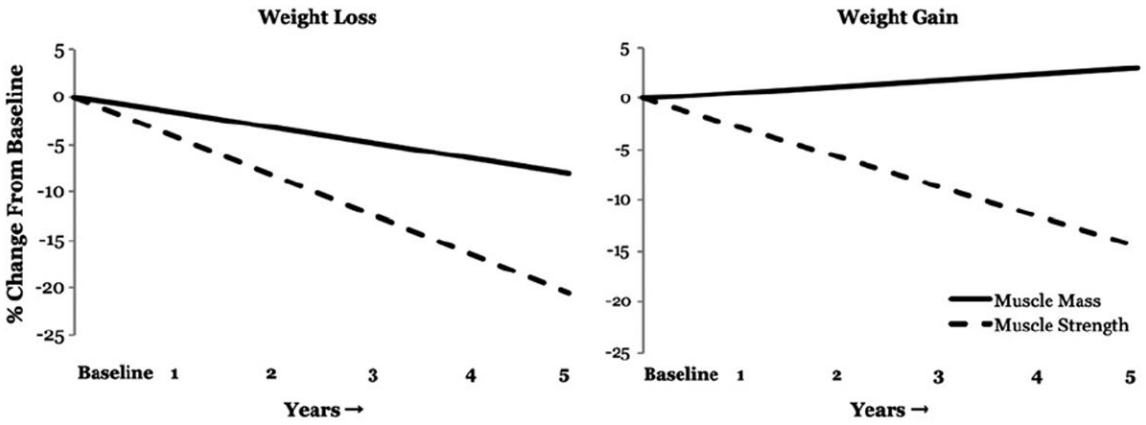

Fig. 2.

The age-related loss of muscle strength is weakly associated with the loss of muscle mass. These figures were adapted from published data obtained from the Health ABC Study to examine the relation between changes in knee extensor strength and quadriceps femoris cross-sectional area muscle (measured by computed tomography) in a 5-y longitudinal study of older adults [15]. These data represent the annualized rate of loss over a 5-y period in older adults who lost body weight (left; n = 309 men) and gained body weight (right; n = 143 men). Note that 1) muscle strength is lost at a substantially faster rate than muscle mass and 2) gaining muscle mass does not prevent the aging-related loss of muscle strength (right). Adapted from data presented by Delmonico et al. [15], with the created figure being approved by the corresponding author (M. J. Delmonico).

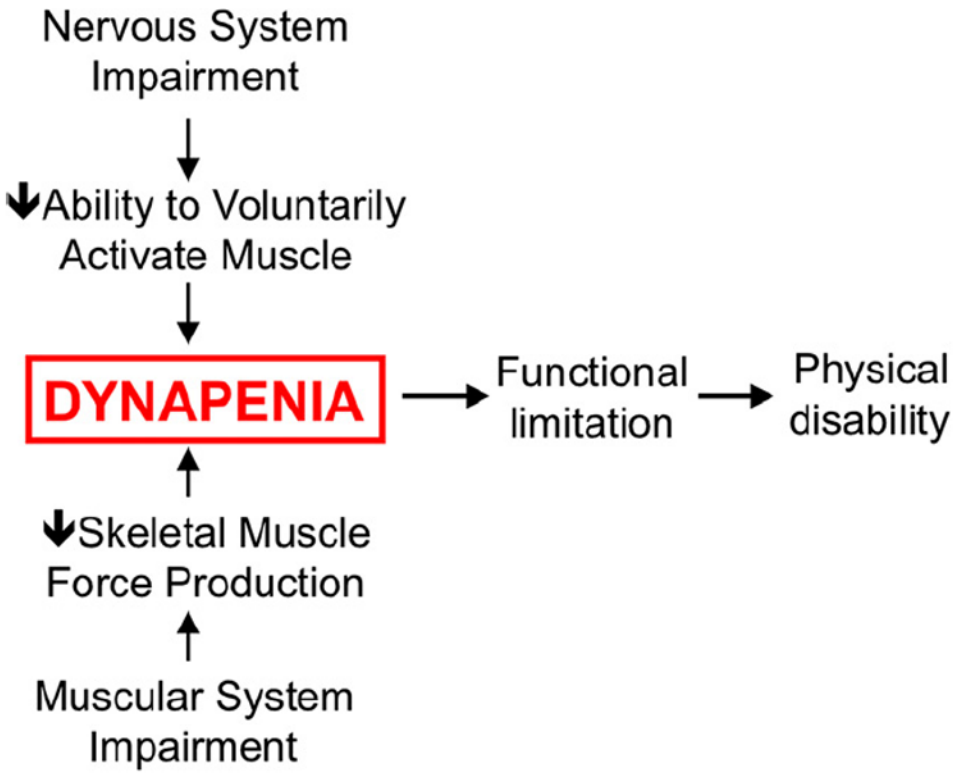

Fig. 3.
Conceptual model of how nervous and muscle system impairments lead to dynapenia.