

Review



Age-related changes in gait biomechanics and their impact on the metabolic cost of walking: Report from a National Institute on Aging workshop

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ABSTRACT

Changes in old age that contribute to the complex issue of an increased metabolic cost of walking (mass-specific energy cost per unit distance traveled) in older adults appear to center at least in part on changes in gait biomechanics. However, age-related changes in energy metabolism, neuromuscular function and connective tissue properties also likely contribute to this problem, of which the consequences are poor mobility and increased risk of inactivity-related disease and disability. The U.S. National Institute on Aging convened a workshop in September 2021 with an interdisciplinary group of scientists to address the gaps in research related to the mechanisms and consequences of changes in mobility in old age. The goal of the workshop was to identify promising ways to move the field forward toward improving gait performance, decreasing energy cost, and enhancing mobility for older adults. This report summarizes the workshop and brings multidisciplinary insight into the known and potential causes and consequences of age-related changes in gait biomechanics. We highlight how gait mechanics and energy cost change with aging, the potential neuromuscular mechanisms and role of

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connective tissue in these changes, and cutting-edge interventions and technologies that may be used to measure and improve gait and mobility in older adults. Key gaps in the literature that warrant targeted research in the future are identified and discussed.

1. Introduction

In old age, reduced or limited mobility, defined here as the ability to move freely in the environment, is associated with a loss of independence and an increased risk of morbidity and mortality (Cooper et al., 2010; Cooper et al., 2011; Guralnik et al., 1995; Studenski et al., 2011). A hallmark of the age-related decline in mobility is a slowing of gait speed; this can also be accompanied by an increase in the metabolic cost of walking (mass-specific energy cost per unit distance traveled) after the seventh decade of life (Schrack et al., 2012), (Fig. 1). Larish et al. (Larish et al., 1988) reported the first observation that walking requires more energy (or caloric expenditure) in older, compared with younger, adults; this was subsequently demonstrated to be consistent across a range of gait speeds (Martin et al., 1992). A higher energy cost of walking is proposed as a risk factor for developing slowed gait speed and reduced mobility in old age (Schrack et al., 2016). However, the mechanisms for this association between gait speed and energy cost are not yet understood, nor consequently have versatile and effective interventions to mitigate this problem been fully developed. The significant societal, economic, and personal burdens associated with mobility limitations highlight the importance of understanding the mechanisms for increased metabolic cost of walking and slowed walking speed with aging.

The United States National Institute on Aging convened a 2-day workshop titled “Causes and Consequences of Age-Related Changes in Gait Biomechanics: The Metabolic Cost of Walking” in September 2021. Given the holistic approach needed to solve the riddle of reduced mobility with aging, the scientists and clinicians invited to participate in this workshop represented the fields of gerontology, epidemiology, physiology, biochemistry, engineering, physical therapy, neuro-mechanics, kinesiology, robotics, rehabilitation, evolutionary biology, and biomechanics. The speakers were charged with the task of distilling the state of science in their field into short, focused presentations that identified current knowledge, key knowledge gaps and emerging opportunities that might be applied to the problem of increased energy cost of walking, gait changes, and consequent mobility limitations in aging. Presentations were followed by small group discussions to identify the most important and targetable gaps that should be addressed in order to move the field forward. These small groups reconvened for whole-group synthesis sessions to bring together the new ideas that the small groups had generated. In this way, the workshop identified areas for future research, innovation, and collaboration to advance knowledge of the multifactorial issue of age-related changes in mobility.

This report synthesizes the current state of the field and highlights

research gaps to be addressed based on the discussion by the assembled group of experts. The discussion topics were not exhaustive but rather focused on the key areas of existing work, and the assembled experts' perception of the most critical areas for future focus. The report is structured similarly to the four main sessions of the workshop: i) age-related changes in gait biomechanics; ii) neuromuscular mechanisms for age-related changes in gait; iii) tendon and connective tissues changes with aging; and iv) interventions and assistive technologies to improve mobility in aging. Discussion related to the importance of increasing diversity and inclusivity in this field of research, as well as the context for the problem provided by two keynote talks, are also highlighted. Overall, the consensus from the workshop was that a more complete understanding is clearly needed to identify how an increased metabolic cost of walking develops in old age, and how that might be mitigated to maintain mobility in our aging population. In understanding the changes in gait and energetics with old age, the context in which gait quality degrades (e.g., uneven terrain), the reasons that gait patterns change (e.g., shift to greater use of proximal muscles) and the impact of study activities that may be novel for participants (e.g. treadmill walking) (Das Gupta et al., 2019) are essential to consider. Finally a suggested aim of future research should be to understand how age-related challenges to mobility develop, and how best to maintain mobility and health throughout the lifespan.

2. Session 1: changes in gait biomechanics with aging

A prevailing concept in the field of gait biomechanics is that there is a “distal-to-proximal shift” in muscle workloads with advancing age such that older adults move away from an “ankle strategy” toward a “hip strategy” for producing propulsion and support during walking (Boyer et al., 2017; DeVita and Hortobagyi, 2000) (Fig. 2). For example, older adults produce less power at the ankle than younger adults at push-off during both level and uphill walking (Buddhadev and Martin, 2016; Franz and Kram, 2014). When gait speeds are matched, older adults also produce more power at the hip than younger adults (Boyer et al., 2017). Moreover, the greater reliance on hip muscles for walking in older adults was found to be a significant predictor of the greater metabolic cost in older as compared to younger adults (Delabastita et al., 2021). Elevated metabolic cost with a shift from reliance on distal to proximal muscles is consistent with modeling results showing that the plantar flexors function with relatively low energy cost in walking due, in part, to effective storage and release of elastic energy in the Achilles tendon (Umberger and Rubenson, 2011). However, a full understanding of the changes in neuromuscular control responsible for the redistribution of joint

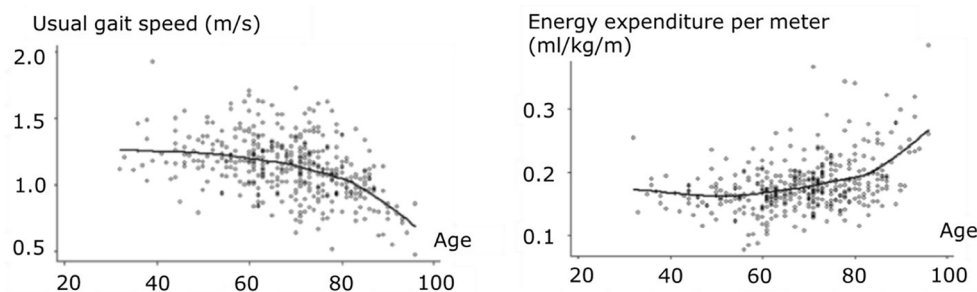


Fig. 1. A cross-sectional analysis from the Baltimore Longitudinal Study of Aging shows that walking speed remains relatively constant throughout adulthood until the 7th decade, when usual gait speed begins to decline (left). The curvilinear relationship between Usual gait speed and age is shown with a lowess fit curve. Age-related changes in energy expenditure (right) mirror the changes in walking speed, suggesting an association between usual walking speed and age-related changes in energy use during locomotion. The curvilinear relationship between energy expenditure and age is shown with a lowess fit curve. Figure adapted from

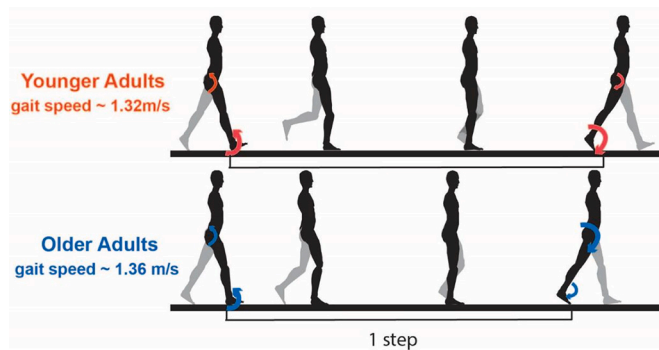


Fig. 2. With age, both joint motions (kinematics) and causes of motion (kinetics) differ from those of young adults. Compared with younger adults, older adults, even at speeds matched to the young, walk with shorter strides, cover less distance with each step, have greater double support time and have smaller joint ranges of motion, particularly at the ankle and sometimes the hip. At the end of a step, older adults have greater hip joint moments and powers (large arrows), but smaller ankle moments and powers compared to younger adults (small arrows). Figure based on data from Boyer et al. (Boyer et al., 2017).

mechanical powers in older adults remains elusive (Peterson and Martin, 2010). There are limited data for how activation patterns of specific muscle and muscle groups change with age and contribute to the above-mentioned gait changes. For older compared with younger adults, differences including greater levels and prolonged timing of antagonist muscle co-activation have been reported (Peterson and Martin, 2010; Hortobagyi et al., 2011; Hortobagyi et al., 2009) and appear to be related to the greater cost of walking in aging (Peterson and Martin, 2010; Hortobagyi et al., 2011; Franz and Kram, 2013; Ortega and Farley, 2015). Further knowledge of the nature, causes, and consequences of age-related changes in neuromuscular control is needed to inform interventions targeting problematic alterations in gait with aging. The discussions at the workshop were focused on understanding limitations in our current knowledge of what “aged gait” is, the proposed mechanisms for the observed changes, as well as new scientific approaches and tools available that may be helpful in advancing the science in this area.

The nature and magnitude of age-related biomechanical adaptations are complicated by factors such as habitual physical activity and self-selected walking speed. Many studies compare gait kinetics and kinematics in younger and older adults, which can be an appropriate study design. However, these cross-sectional studies often find that both groups have a similar preferred walking speed, suggesting that the field is most often examining a highly mobile subset of older adults that may not represent the target population: older adults at risk for or living with walking impairments. Future studies need to include older adults with slowed gait speeds and incident mobility limitations, as these individuals may represent a population of people that often does not make it into laboratories for research studies, but is representative of a large proportion of adults in the community. Indeed, there is merit to comparing low-functioning older adults with high-functioning older adults using a case-control study design.

The mechanisms for altered gait mechanics with age remain unclear. The initial hypothesis has been that reductions in maximal muscle force or power prompt a need to alter gait mechanics in order to avoid approaching the maximal capacity of any one muscle group. However, while healthy, mobile older adults typically produce less positive joint power and work at the ankle, when given biofeedback about their performance they have the capacity to produce similar propulsive power at the ankle as younger adults (Browne and Franz, 2019). Functional demand (i.e., the ratio of external joint kinetics to maximal muscle torque) for both the plantar flexor and knee extensor muscle groups is larger in older compared with younger adults (Spinoso et al., 2019; Samuel et al., 2013), and overall functional demand increases as walking speed increases (Hafer and Boyer, 2020). Might these differences in functional

demand explain greater energy cost and slowed gait speeds in aging? Do these results extend to older adults already experiencing mobility limitations? Estimates vary considerably, however, functional demand generally does not exceed or even approach the maximum capacity for most locomotor muscle groups. In addition, differences in gait mechanics have been reported in mid-life adults (50–64 years) prior to the generally expected onset of age-related declines in muscle function (Boyer et al., 2012; Jin and Hahn, 2019). Notably, several studies report no gait differences between older adults with higher levels of physical activity and, presumably, more “youthful” muscle function than those with low habitual physical activity levels (Krupenevich and Miller, 2021; Hafer et al., 2019). The concept that muscle power, which involves not only the force produced but also the velocity of the contraction, is a better predictor of future morbidity than torque alone has gained substantial support in recent years (Bean et al., 2003; Losa-Reyna et al., 2022). While muscle strength (i.e., maximal voluntary torque) is likely to play some role in the alteration of gait with age, looking beyond muscle strength alone to evaluate the impact of changes in structure, composition, and morphology of muscle and tendon (Krupenevich et al., 2021); contraction velocity and power (Bean et al., 2003); neural drive to muscle (Clark et al., 2014); and interactions among these systems may yield more insight about the mechanisms of age-related changes in gait mechanics.

Tendons work in concert with muscles; therefore, the entire muscle-tendon complex should be considered when exploring the mechanisms for changes in gait biomechanics with aging, and their consequences on the metabolic cost of walking. Advances in ultrasound techniques have yielded new observations of changes in Achilles tendon behavior with age. There is evidence of less independent movement of the subtendons during gait for older adults (Franz and Thelen, 2016), which may contribute to the lower propulsive power observed at the ankle in older adults (Rasske and Franz, 2018). Differences in Achilles tendon moment arm and stiffness may also impact the propulsive power at the ankle and metabolic cost of walking for older adults; however, these are not consistent findings (Delabastita et al., 2021; Franz and Thelen, 2016). The Achilles tendon has more capacity for storing and returning elastic energy than do the tendons about the knee and hip, which may help explain, in part, why a “hip strategy” is a less economical way to ambulate (Umberger and Rubenson, 2011; Sawicki et al., 2009). While additional evidence is needed to quantify the role of altered muscle-tendon unit properties on gait mechanics, addressing these changes in plantar flexor muscle tendon unit behavior and propulsive power at the ankle is one potential strategy that could be explored to understand changes in the metabolic cost of walking in the old. Biofeedback or exoskeletons may be useful experimental models for exploring these questions (Browne and Franz, 2019; Jackson et al., 2017). Without this information, questions will persist as to: the optimal training strategy to improve propulsive power, particularly in those with reduced mobility; when to intervene; and how to maintain these adaptations to decrease the cost of walking and preserve mobility throughout the lifespan. Indeed, a better understanding of causes of changes to gait in aging is needed before effective interventions can be designed (Beijersbergen et al., 2013).

Likewise, strategies intending to reverse age-related changes in gait mechanics must take into consideration the priorities of the individual, along with the effect that targeting a specific biomechanical deficit may have on overall mobility and quality of life in older adults. For example, stroke is a condition that affects almost one million Americans every year (Virani et al., 2020), the majority of whom are over the age of 65 years. Recovery from stroke often involves physical rehabilitation to regain strength and mobility, and studies have shown that people can improve their walking symmetry post-stroke (Wist et al., 2016). However, this increased gait symmetry did not improve the energy cost of walking (Sánchez and Finley, 2018), and may have had a negative impact on balance (Park et al., 2021). Further, although slowed gait speed is considered problematic (as, for example, when crossing a busy

street), interventions designed to increase gait speed may also have a negative impact on balance in some people, depending on their strategy for increasing speed (Espy et al., 2010). Thus, the goal of a rehabilitation program for a given individual may need to be adjusted to exploit and optimize the residual mobility function by training positive compensatory adaptations, rather than necessarily to restore kinematics or speed to an earlier state. In many situations, personalized solutions may be essential. Thus, the field should focus on establishing methods for determining optimal rehabilitation outcomes for individuals based on their goals, needs, limitations, conditions, and environment.

To optimally target and ameliorate age-related changes in gait biomechanics and their effects on the metabolic cost of walking, the specific mechanisms underlying these changes must first be understood. It is often difficult to identify causal relations in biological systems using experimental approaches alone. In the context of understanding age-related gait changes, there are many potential confounding factors, such as muscle weakness, altered neural drive, and decreases in tendon stiffness that may co-vary and interact in complex ways. Computational modeling and simulation (Fig. 3) could be integrated with experimental data to better understand the potential impact of each factor on gait in isolation, as well as the nature of their interactions (Umberger and Rubenson, 2011; Fernandez and Pandy, 2006). However, this approach has been applied only sparingly to the questions of muscle-tendon function (Franz and Thelen, 2016; Hasson and Caldwell, 2012; Thelen, 2003) and gait biomechanics (Song and Geyer, 2018; Pimentel et al., 2021; Hase, 2008; Lim et al., 2013) older adults. Thus, there is considerable unmet potential in using musculoskeletal modeling and simulation to help identify the biological changes that occur with aging that are most responsible for observed changes in gait biomechanics and the metabolic cost of walking.

Human locomotion has been simulated using two major approaches that involve so-called tracking simulations and predictive simulations (Umberger and Miller, 2018). *Tracking simulations* that reproduce experimental data are useful to help understand muscle function (Lim et al., 2013), and are complementary to experimental analyses based on joint kinematics, kinetics, and electromyography. However, *predictive simulations* hold considerably more potential for identifying the causes of age-related gait changes. Predictive simulations generate novel movements based on the characteristics of the model (Umberger and Miller, 2018). Thus, it is possible with predictive simulations to identify how particular age-related changes in static properties (e.g., muscle strength, joint range of motion) and dynamic properties (e.g., muscle contraction speed, neural conduction speed) of the neuromusculoskeletal system precipitate specific changes in gait performance (e.g., increased metabolic cost of walking, decreased gait speed, impaired dynamic balance), (Fig. 3), and thereby provide useful information about which

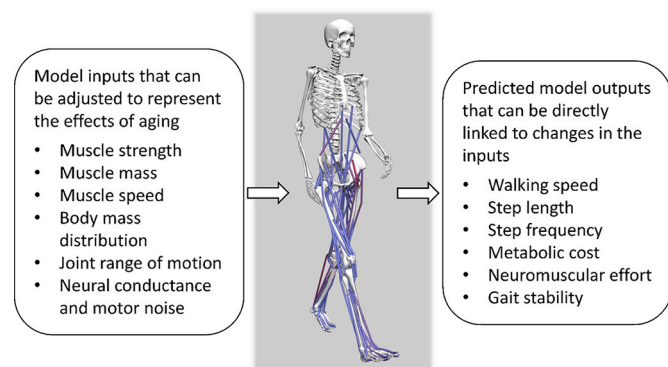


Fig. 3. Musculoskeletal modeling is a powerful approach for testing cause-and-effect relations in human movement. In the context of understanding the causes of age-related changes in gait mechanics and energetics, several model inputs (left box) can be adjusted to predict the relative magnitudes of their effects on model outputs (right box). Figure courtesy of B. Umberger.

interventions are likely to be most effective at restoring performance (Song and Geyer, 2018; Ong et al., 2019; Johnson et al., 2022).

While computational modeling holds considerable promise, challenges remain to maximize its utility as a tool to help solve the broader problem of poor mobility with aging. Key among them is that predictive simulations require the objective or goal of the movement task to be specified, such as weighting metabolic cost against gait stability or movement smoothness (Umberger and Miller, 2018; Nguyen et al., 2019). This is an active area of research that must be expanded to include older adults who are, for example, at greater risk of falls and thus may place a greater personal priority on stability than energy cost. Importantly, the field also needs to identify how to best integrate the results of simulation studies with other sources of evidence, such as experimental and epidemiological data, to better understand the primary causes of age-related gait impairments and develop effective, targeted interventions.

In sum, there exist significant knowledge gaps (Table 1) and therefore great potential for future research to advance our understanding of age-related changes in gait and the metabolic energy cost of walking. Multidisciplinary research that integrates experimental studies with mechanistically-focused approaches to capitalize on new technologies is essential to progress in this area. Consideration of study cohort characteristics and their goals will be needed, as will a better understanding of underlying changes before effective interventions can be developed. The next sections examine several factors that have been identified as critical to our understanding of aging, gait, and the metabolic cost of walking.

Table 1

Knowledge gaps and areas of opportunity for advancing the science investigating the increased energy cost of walking in old age.

| Topic | Knowledge gap |
|----------------------------|--|
| Gait biomechanics | Magnitude and mechanisms of distal-to-proximal shift in gait patterns Mechanisms of increased metabolic energy cost of walking in older people At what age and in whom is metabolic energy cost of gait higher? Impact of various moderators including sex, habitual physical activity etc. Gait alterations and impacts in diverse study groups, including those with slowed self-selected gait speed, incident mobility limitations, etc. Mechanisms for greater antagonist muscle activation Real world measurement of aged gait and impact of environment |
| Neuromuscular factors | Effects of fat deposition and distribution Nervous system changes: effects on coordination, synergies, and speed and completeness of activation Role of weakness and fatigue in gait and metabolic energy cost changes |
| Tendon & connective tissue | Role of muscle tendon complex in gait changes and greater cost of walking? At which joints? What are the changes, mechanisms and impact of age-related alterations in the extracellular matrix in vivo? |
| Interventions & sensors | Clinical targets vs. personalized goals? Pros and cons of assistive devices vs. capacity-building interventions Sensors or devices for detection of early changes that may lead to gait problems Design and deployment of sensors to track long-term changes, with sufficient data richness and high usability How to scale to population level? |
| Study design | Which problems are common across various sectors of aging population? Effects of age, sex, health status, physical activity level, etc.? Integration across scales, systems and approaches Adoption and compliance; cultural, racial and gender needs |

3. Session 2: neuromuscular mechanisms for changes in gait biomechanics

The aging human neuromuscular system undergoes normative changes beyond loss of muscle mass and strength that may also contribute to reduced mobility, although in many cases the specific mechanisms for these changes and their direct impact on gait biomechanics have not yet been fully identified. For example, body mass increases with age up to about age 80 years, due to an increase in fat mass and despite a loss in lean mass in males (Jackson et al., 2012) and females (Kemper et al., 2021). To fully understand gait changes with aging, particularly as they relate to metabolic energy cost, it is important to clarify why changes in body composition occur over time and how they influence mobility. Importantly, there is little association between low muscle mass and functional decline with age, although muscle strength is a strong predictor of functional decline (Schaap et al., 2013). Rather, fat accumulation is more strongly associated with age-related mobility impairment than is loss of lean mass (Kidde et al., 2009). Further, fat *distribution* may have an even greater impact on mobility than overall fat *accumulation*. There is an age-related redistribution of fat away from subcutaneous fat and toward internal organs and tissues, including skeletal muscle (Delmonico et al., 2009). Notably, it has been shown that fat within skeletal muscle tissue is the greatest body composition risk factor for slower gait speed and mobility disability (Beavers et al., 2013) (Fig. 4). Thus, it is critical to understand how changes in fat distribution may affect mechanical or bioenergetic factors to impact gait and mobility in aging. Likewise, the interaction between or ratio of lean mass to fat mass and its role on strength or power, which is strongly associated with reduced physical function in aging (e.g., Suetta et al., 2019)), needs more nuanced understanding. The question of causality vs. association must also be addressed in order to understand the mechanistic roles of muscle weakness and fat accumulation and distribution on gait mechanics and the cost of walking in old age.

The aging nervous system undergoes substantial changes that likely affect the ability of older adults to be active and mobile in their daily lives. The predictive role of low muscle strength and power on functional decline with aging (Schaap et al., 2013) suggests that either reduced muscle mass or an inability to optimally activate muscle could play a role in altered gait mechanics with aging. Documented changes in the nervous system with aging that may affect activation of available muscle include brain atrophy, changes in motor cortex excitability, axonal damage (Pratt et al., 2022), neuromuscular junction damage (Pratt et al., 2022), and muscle denervation (Mosole et al., 2014) leading to a loss of motor units (Hunter et al., 2016). Central nervous system

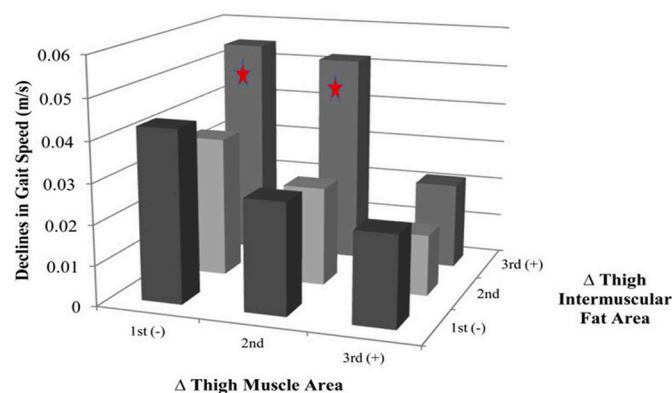


Fig. 4. Accumulation of intermuscular fat is an important risk factor for slowing gait speed and loss of mobility in aging. Health, Aging and Body Composition Study participants with the greatest decreases in thigh muscle area but increases in thigh intermuscular fat area experienced the greatest declines in gait speed over a 4 year period. 1st, 2nd, and 3rd refer to tertiles. Figure courtesy of B. Nicklas and Beavers et al. (2013).

alterations that may be deleterious to gait such as agonist co-activation and altered muscle synergies also occur with aging (Manini et al., 2013; Mooney et al., 2014; Piche et al., 2022), although the extent to which these are direct effects of aging or indirect effects of inactivity and disease is not clear at present. Regardless, these changes can lower the ability of muscle to produce force and power, and they appear to impact the control of walking and coordination during the various phases of gait (Song and Geyer, 2018; Hafer et al., 2016; James et al., 2016). There are emerging opportunities to solidify knowledge relating cognition and changes in cognition with age to the variability, complexity and stability of gait, as well as the implications of these factors for mobility. Research in this area should also expand on work in younger adults that has shown a link between gait variability and the metabolic cost of walking (O'Connor et al., 2012). Degradation of the sensory system also occurs with aging, and can lead to deficits in eyesight, proprioception, vestibular sensing, and cutaneous sensing (Allen et al., 2016). Neither the ability of the aging nervous system to adapt to unanticipated challenges or dual tasks during walking, nor the impact of poor sensorimotor function on gait have been resolved. It will also be important to understand how nervous system changes impact skeletal muscle function in its role of supporting locomotion.

An increased metabolic cost of walking with age may have multiple causes, including muscle weakness, slower preferred gait speeds, and altered muscle activation patterns, as discussed above. More directly, greater metabolic cost during gait may also be related to impaired cellular energy metabolism. Intramuscular energy production can be studied noninvasively using phosphorus magnetic resonance spectroscopy. To date, we know that the effects of older age on skeletal muscle oxidative or mitochondrial capacity in vivo vary depending on the muscle group and participant characteristics (Fitzgerald et al., 2016). For example, a meta-analysis of the literature revealed that the dorsiflexor muscles of older adults have a greater capacity to produce energy (i.e., ATP) by oxidative phosphorylation than do those of younger adults, a result that may be related to a relatively greater duty cycle in this muscle group during the altered gait of older adults. In contrast, the knee extensor muscles were the only muscle group to show a lower oxidative capacity in older compared with younger adults (Fitzgerald et al., 2016), an effect exacerbated in older adults with mobility impairments (Larsen et al., 2012). Indeed, cross-sectional and more recently longitudinal studies of the quadriceps muscles in the Baltimore Longitudinal Study of Aging have shown that post-exercise oxidative capacity in muscle declines with aging, even when healthy individuals are studied (Choi et al., 2016; Adelnia et al., 2020). Independent of age and confounders, oxidative capacity is associated with reduced walking speed, especially in tasks that require endurance, such as the 400 m walk. In mediation analysis, this association is explained by lower muscle strength (Tian et al., 2022; Tian et al., 2021; Zane et al., 2017). Habitual physical activity level is also a significant moderator of muscle oxidative capacity (Fitzgerald et al., 2016; Larsen et al., 2012). The causal nature of the relationship in older adults between a muscle's daily usage patterns and its ability to produce energy oxidatively remains to be determined.

In addition to evaluating muscle oxidative *capacity*, it is useful to determine the *use* of each ATP-producing pathway (i.e., creatine kinase reaction, glycolysis, oxidative phosphorylation) during muscular work. Studies of single muscle groups in vivo suggest that under some conditions, older muscle relies relatively more on oxidative metabolism than younger muscle (Lanza et al., 2007; Christie et al., 2014), but this difference is difficult to ascertain during locomotor tasks. Perhaps most relevant to the question of the energy cost of walking, a recent study of knee extensor muscle metabolic economy (torque or work per ATP per unit muscle) indicated similar economy in young and older adults during isometric contractions, but far lower economy in the old during dynamic contractions (Fitzgerald et al., 2021), (Fig. 5). This scenario is consistent with a greater metabolic cost of walking with aging, and suggests that intrinsic muscle factors may contribute directly to this problem in older

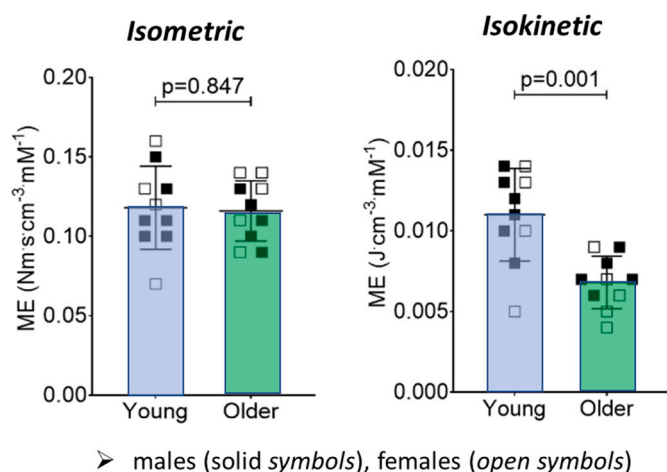


Fig. 5. Knee extensor muscle metabolic economy (size-normalized torque or power produced per mM ATP) is lower in vivo during dynamic, isokinetic (right) but not static, isometric (left), contractions in older compared with younger adults. Dynamic contractions were performed at 120 deg.·s⁻¹. Both conditions involved maximal, single-leg contractions on a magnetic resonance compatible ergometer. The potential impact of lower muscle economy on the increased energy cost of walking in aging remains to be determined. Figure adapted from Fitzgerald et al. (Fitzgerald et al., 2021).

adults. Further, the consequences of lower skeletal muscle economy on muscle fatigue and whole-body fatigability (discussed next), which in turn may exacerbate gait changes in the old, need to be clarified. Given concepts such as the distal-to-proximal shift in gait kinetics with aging, future emphasis should be placed on understanding how energy is produced and used in the hip extensor muscles. Studies that combine measures of in vivo energetics and economy with computational models may prove valuable in identifying specific responses and muscle groups that are contributing most to the greater energy cost of walking in older adults (Callahan et al., 2013).

While *muscle fatigue* is defined as the transient loss of maximal force- or power-generating capacity of muscle in response to its use (Kent-Braun et al., 2012), the emerging concept of *fatigability*, or the decline in physical performance in response to a standardized bout of activity (Eldadah, 2010; Simonsick et al., 2016; Alexander et al., 2010), has important implications for the age-related decline in mobility. It is well known that muscle fatigue is task-specific, meaning that the magnitude and mechanisms of fatigue will vary depending on the intensity, mode and duration of the contraction protocol used to elicit it (Kent-Braun et al., 2012; Enoka and Duchateau, 2008). For example, for isometric tasks of the lower limb muscles, healthy and mobile older adults are typically less fatigable than young adults but are more fatigable for dynamic contractions, particularly as contraction velocity increases (Dalton et al., 2012; Paris et al., 2022; Callahan and Kent-Braun, 2011; Sundberg et al., 2018). The mechanisms for greater muscle fatigue in older adults during dynamic contractions of single muscle groups appear to include the muscle's failure to keep pace with the high energy demand of these contractions (Sundberg et al., 2019). In addition to contraction mode and muscle group; sex, age and habitual physical activity are potent moderators of muscle fatigue in aging (Christie et al., 2011). The extent to which locomotor muscle fatigue contributes to overall fatigability or the decline in physical performance is unclear at present. Future studies should continue to identify the causes and consequences of skeletal muscle fatigue in all sectors of the aging population, especially as it relates to locomotor tasks, the concept of fatigability, and changes in the metabolic energy cost of walking.

4. Session 3: connective tissue function in aging

Connective tissue, including tendons and the extracellular matrix,

transmits the forces generated by muscle fibers and acts as a spring during locomotion. As discussed above, despite the key role of connective tissue in locomotion and gait, potential age-related changes in connective tissue function with aging have received relatively little attention to date, particularly in humans. Both the material and mechanical properties of tendon may undergo age-related changes. In adults, tendons are composed predominantly of type I collagen fibers, which provide the tensile, load-bearing properties of the tissue. Other components of tendons include type III and type IV collagens, proteoglycans, and fibroblasts (Svensson et al., 2016). Animal studies provide the majority of information about changes in material properties of tendons with age, and mainly indicate a decrease in cell density during maturation to old age, and should account for age-related changes in behaviors such as physical activity. Creative approaches to study the material properties of human tendons should also be explored, including developing new techniques to obtain tissue samples with minimal risk to participants or obtaining tissue during elective surgical procedures. Ultrasound-guided tendon tissue sampling techniques may provide a way to obtain human tendon tissue from the patellar and Achilles tendons (Movin, 2000).

There are known age-related changes in tendon properties. Older adults demonstrate lower Achilles tendon stiffness (Onambele et al., 2006), smaller Young's modulus, increased hysteresis (Reeves et al., 2003) and greater tendon cross-sectional area than younger adults (Lindemann et al., 2020; Stenroth et al., 2012) (Fig. 6). However, in the patellar tendon, the results are mixed. One early study reported no differences between older and younger adults in patellar tendon properties (Carroll et al., 2008). However, more recent data in older males indicates both lower tendon stiffness than younger males and a direct association between patellar tendon stiffness and rate of force development during maximal isometric contractions (Quinlan et al., 2018). The mechanisms for these changes in tendon properties or lack thereof and the role of changes in magnitude and frequency of loading should be explored further. In addition, the potential effects of sex hormones on age-related changes in tendon stiffness and, in turn, the effects of stiffness on the rate of force development are not known but may be highly relevant to the question of aging. The changes in tendon properties may directly impact the energetic cost of locomotion by impacting the elastic energy return but may also increase the metabolic cost of walking by impacting function of the muscle-tendon complex including the muscle fascicle length, rate of force development, and electromechanical delay (Krupenevich et al., 2021; Svensson et al., 2016; Bojsen-Møller et al., 2005).

Investigators have begun to explore the effects of age-related changes to the mechanical properties of tendon on mobility in older adults. Stenroth et al. (Stenroth et al., 2015) reported significant associations between 6-minute walk time and Achilles tendon stiffness in older adults. Few studies have examined tendon mechanical properties during mobility tasks in older adults. Overall, research has shown that the mechanical properties of the tendon affect muscle fascicles during the gait cycle (Conway and Franz, 2020). During walking, older adults have altered muscle-tendon complex lengthening during the stance phase, such that increased tendon compliance is accompanied by reduced fascicle lengthening compared to younger adults (Mian et al., 2007). Older adults also experience smaller peak tendon stress during push-off in walking compared to younger adults (Ebrahimi et al., 2020). The implications of age-related changes in tendon mechanical properties for altered self-selected gait speed and metabolic cost of walking in older adults is likely significant but not well understood. Advances in technology that enable measurement of tendon loading during locomotion may support this new line of research (Harper et al., 2020). There is some evidence to indicate that tendon properties can be modified

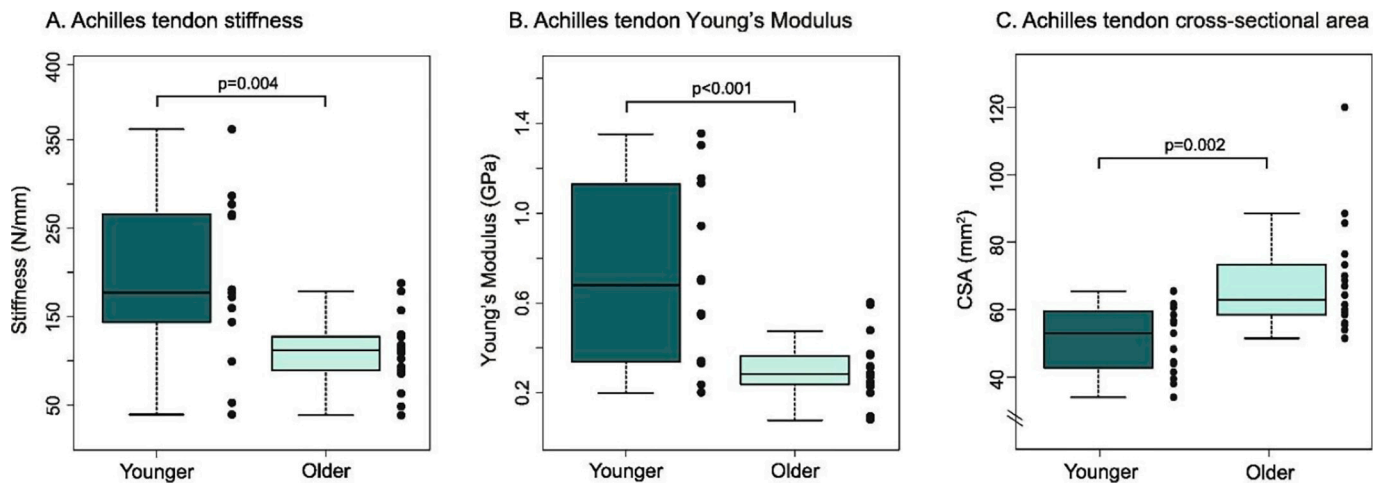


Fig. 6. Achilles tendon stiffness (*left*) and Young's Modulus (*center*) are both lower in older adults with similar physical activity patterns to younger adults. Notably, tendon cross-sectional area is greater in the old (*right*), which is suggested to be an adaptation to counter reduced material modulus in the tendon. Figure from Lindemann et al. (Lindemann et al., 2020).

through exercise training to optimize mobility in older adults (Reeves et al., 2003; Quinlan et al., 2021). There is emerging evidence of the molecular mechanisms for mechanotransduction in tendon; understanding age-related changes in these mechanisms will be essential for developing exercise therapies (Nakamichi et al., 2022; Passini et al., 2021; Wang et al., 2021). Additional work building on recently-published imaging and genetic engineering approaches in tendon is needed to advance knowledge of the basic mechanisms for tissue property changes with age. Further research is also needed to determine whether changes observed at the tendon translate to changes in the operating length of the sarcomere during static contractions, dynamic contractions, and mobility tasks in vivo.

In addition to the tendon itself, the extracellular matrix (ECM) is an important, although understudied, component of skeletal muscle. The ECM plays a role in force transmission, passive force development, muscle shape changes, gearing, and mechanotransduction (Purslow, 2020). Therefore, a better understanding of how ECM changes in aging constitutes a significant opportunity for improving gait and reducing its energy cost in this population. There are known age-related changes to the ECM of skeletal muscle, including changes to collagen type and cross-linking, collagen content and morphology, fibrosis and stiffening, and a reduced ability to vary gearing (i.e., the ratio of muscle velocity to fiber velocity) (Roberts et al., 2019; Sinha et al., 2020). However, it is not known whether or how age-related changes to the ECM may affect mobility. Likewise, changes to collagen and fluid pressure in muscle can affect passive and active force development (Sleboda and Roberts, 2020; Sleboda and Roberts, 2017), but future research is needed to understand whether this translates to altered gait in aging. In sum, studies are needed that investigate which specific properties of the ECM, such as its content, morphology, or interactions with fluid, affect skeletal muscle function and consequently gait.

5. Session 4: interventions and technologies to measure and improve gait in older adults

A thorough understanding of the age-related changes in biomechanics, and the mechanisms for those changes that lie within the nervous system, skeletal muscle, tendons, and ECM will lead to opportunities for interventions and assistive technologies to allow older adults to be mobile and active in their daily lives. An important consideration when designing interventions to increase mobility in older adults is to identify what the goal(s) should be. That may mean including outcome measures targeting the hypothesized mechanisms, as well as using measures that capture real-world mobility performance. In free-

living environments, measures of a person's mobility in their community can indicate how much someone moves by quantifying metrics such as step counts, speed, locations that a person visited, or activities that a person did. Measures of gait mechanics are less commonly made in the free-living environment, but quantifying mechanics and strategies employed as someone moves through their world, which could be accomplished by using current and future sensor technologies (Fig. 7), may yield critical insights to the problem at hand. For example, motion tracking based on wearable sensors such as wearable inertial measurement units (IMUs) can provide direct measurement of body segment and joint movements while out in the community, including locomotion, activities of daily living, and specific activities such as exercise. In addition, shear wave tensiometry has been developed to understand Achilles tendon kinetics during walking, which also can be deployed in a real-world setting (Harper et al., 2020).

Researchers will need to consider sensor capabilities, hardiness, size, battery life, data storage, ease of deployment, participant burden, status monitoring, and other factors in their study designs. One study showed that participants can wear IMUs on the feet, wrist, and trunk for four weeks, and that voice recordings can be used by participants to mark loss of balance events, which helps researchers reconstruct foot paths and body motions during a loss of balance event (Ojeda et al., 2019). However, IMUs are not without limitations that need to be carefully considered, including the accuracy and precisions of the selected outcomes. Further advances through sensor fusion to combine kinematic and kinetic measures in the field will make it possible to understand how patterns of motion alter tissue loading in vivo (Harper et al., 2022). Sensor technology is rapidly developing to aid in understanding mobility function both within and outside the laboratory, and in a variety of populations. It will be important to establish and maintain collaboration with computer and data scientists for the interpretation of the complex datasets that will be generated by these studies. Integrative team science approaches that combine researchers with topically diverse backgrounds will be particularly useful in this realm.

Sensor technologies will provide a significant opportunity for guiding the development and evaluation of interventions to improve mobility in older adults. For example, a task-oriented motor learning program that takes advantage of active sensor technologies may improve mobility in older adults by improving the skills needed for walking (Brach and VanSwearingen, 2013). Different approaches may be needed for those with sensory or vestibular deficits than for those with fatigability or sarcopenia. It will be essential to be able to best match an individual's deficits and goals with the most efficacious intervention(s) to improve walking and mobility. Finally, attention must

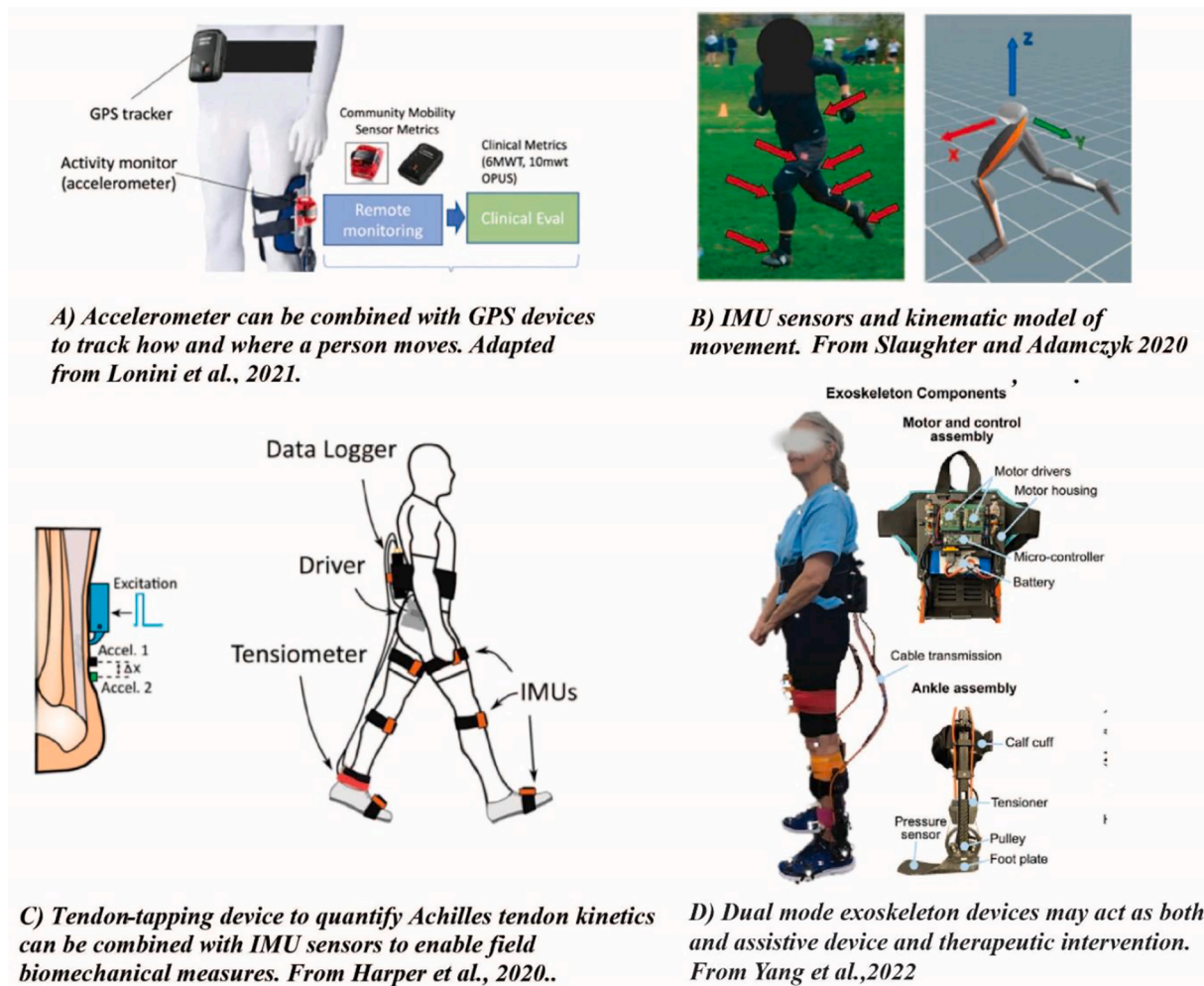


Fig. 7. Measurement of everyday movement can include not only A) how much an individual moves (e.g., step counts, activity intensity, locations) Figure from Lonini et al. *IEEE TNSRE* (Lonini et al., 2021), but also B) the pattern of an individual's movements (e.g., kinematics, muscle coordination) Figure from Slaughter et al. *Sensors* (Slaughter and Adamczyk, 2020), and C) the effects of movement on tissue strain patterns Figure from Harper et al. *Sensors* (Harper et al., 2020). Everyday motions such as walking or chair rising are typically repeated multiple times each day, reducing the barriers to their measurement. In contrast, events such as falls and slips are unique and present a far greater challenge for their identification and study. D) Exoskeleton devices that can switch between assistance and resistance modes may enhance mobility while also acting as a therapeutic intervention to help maintain muscle and tendon function. Figure from Yang et al. *Wearable Technologies* (Fang et al., 2022).

be paid to the behavioral issues of perceived needs, motivation, and compliance in order to design effective interventions.

Cognitive impairment is associated with the risk for mobility limitations in older adults (Buchman et al., 2011); but causality has not been established. Brain aging, including structural and physiological changes, may be a central mechanism affecting both cognition and the neural control of walking. The cognitive domain of executive function may be particularly important, especially for performance of challenging/complex walking tasks (Chatterjee et al., 2019). To date, research has shown that exercise training induces neural changes to the central nervous system (Dishman et al., 2006; Hortobagyi et al., 2022), but a 2018 meta-analysis showed that cognitive training may only improve mobility during challenging walking tasks in older adults (Marusic et al., 2018). Additional, rigorous studies are needed to show whether exercise training can induce neural changes that directly improve mobility in older adults. To this end, comparative effectiveness randomized controlled trials are needed to assess the ability of cognitive-motor interventions, ideally those that target both cognition and motor function, to reduce mobility disability. As a first step, the feasibility of such trials should be evaluated. Studies will also be needed to examine the mechanisms that explain how cognitive-motor therapies improve motor function in older adults. Quantification of mobility behavior, gait

mechanics, muscle-tendon function, brain and muscle activation, energetic cost of walking and detraining effects (Hortobagyi et al., 2021) should all be thoroughly investigated in the context of motor-cognitive therapies.

In addition to interventions designed to modify or improve the innate functional capabilities of older adults, assistive devices may be able to improve gait function in older adults in specific situations, especially if capacity or components of gait cannot be restored with rehabilitation. Traditional assistive devices to improve mobility include canes, crutches, walkers, and rollators (Bertrand et al., 2017). Scientific advances have allowed for the development of exoskeletons as a walking aid to improve gait function and reduce the metabolic cost of walking (Sawicki et al., 2020). The first exoskeleton to break the metabolic cost barrier was an ankle exoskeleton that assisted plantar flexion; it required a power source and had to be used in a laboratory setting, but it showed that an exoskeleton could reduce the metabolic cost of walking (Malcolm et al., 2013). Since then, scientists have continued to develop exoskeletons as walking aids. For example, exoskeletons have been developed that are autonomous, meaning that they are untethered and self-contained when worn by a person (Mooney et al., 2014). Exoskeletons have also been developed that are passive, meaning that they do not require an input of energy (Collins et al., 2015). While these

developments are promising, many questions remain before exoskeletons might be widely used in the aging population. First, the best methods of exoskeleton use will need to be established. For instance, it is unclear which lower-limb joint (i.e., hip versus knee versus ankle) is the best target for intervention, and whether this depends on the aspect of mobility that the device is intended to address (e.g., metabolic cost, self-selected walking speed, or balance). The intensity and frequency of use is also uncertain; would it be most effective to use an exoskeleton periodically to train gait and restore mobility, continuously to augment gait in daily life, or by balancing these two approaches? The question of whether “too much” use of an exoskeleton might contribute to atrophy and deconditioning must be addressed and raises the possibility of exoskeletons that can switch between assistance (i.e., to help reduce metabolic cost or increase self-selected walking speed) and resistance (as a therapeutic intervention to help maintain muscle and tendon function) modes (Fang et al., 2022) (Fig. 7). The complexity, cost and regulatory burden of demonstrating clinical efficacy of exoskeletons might limit their utility and scalability to large segments of the population. A simple, passive hip exoskeleton was developed to overcome cost and complexity concerns. It was shown to reduce the cost of walking in older adults in a laboratory setting (Panizzolo et al., 2019), but its use in a real-world setting is as yet unproven. The possibilities for exoskeletons to improve mobility for older adults are immense, but their use for all older adults, including those with comorbidities, neuromuscular disease, injuries, or cognitive impairment, is uncertain at this time.

6. Session 5: considerations for inclusive study design

Moving the field forward toward understanding gait and improving mobility in our aging population will require research that is much more inclusive and diverse than has been common to date. Too frequently, convenience samples from local university communities fail to study people from diverse socioeconomic, racial, ethnic, educational, occupational, and ability backgrounds. Problems generated by a lack of diversity include, for example: uncertainty about how genetic vs. behavioral factors affect the aging process and thus the mechanisms and outcomes related to gait and energetics, or the development of monitoring strategies and interventions that may not be appropriate across all subpopulations.

To increase diversity and inclusion, community partnerships should be forged that are mutually beneficial to community members and researchers. The Johnson County Osteoarthritis Project offers an example of one such successful community partnership (Hartman et al., 2007). This community-based participatory research project incorporates diversity into its study design in order to engage those individuals at high risk for developing osteoarthritis. Indeed, including stakeholders in pre-study planning, such as diverse patients from the study population of interest, clinicians, caregivers, etc., may help ensure that interventions meet their needs and are implemented in ways that can increase adoption of and compliance with the study goals and design. Despite some successful partnerships in the field of mobility and aging, there remain many unanswered questions about how to facilitate such partnerships, as well as how to interpret results that differ by race or other subgroup. Collaborations with, for example, social scientists, clinical researchers and/or biologists may be important for interpreting data to inform future interventions or advance care for specific populations.

One challenge that the workshop participants thought should be addressed is to identify ways to improve inclusivity in research, such as including all people who are interested in participating in these studies. Stringent inclusion and exclusion criteria are important for creating homogenous research groups in order to tease out differences between groups; however, eligibility criteria may be preventing certain groups of people from being represented in research studies. For example, among adults over 65 years of age, those without disease or disability are often overrepresented in research studies due to their overall good health, relatively good mobility status, and low burden of comorbidities. From a

clinical perspective, we can look to the field of geroscience for guidance on addressing variability in responses to exercise intervention programs. Geroscience is the field that aims to understand the basic physiology of aging to explain the increased occurrence of age-related diseases throughout the lifespan (Kennedy et al., 2014). Insights from geroscience and “life course epidemiology” may suggest cellular and molecular targets that allow researchers to identify people at risk for mobility impairments and, further, to identify personalized interventions or novel therapeutics for improving mobility (Ferrucci et al., 2016).

In addition, clever statistical designs, sharing of data between research groups to create larger datasets, and team science may be important approaches for overcoming the inevitable variability that will be introduced through loosening eligibility criteria to include a more representative sample of the aging population. To that effect, the establishment of a common core set of outcome variables would create unity between research studies and allow for compilation of data and greater comparison of data collected in different laboratories. Further, these measures should be accessible to the majority of researchers, meaning that they can be performed just as easily in small rural laboratories or field sites as in large urban research centers.

7. Conclusion

The 2021 National Institute on Aging workshop on the causes and consequences of altered gait and increased metabolic energy cost in aging identified key areas where research should be focused in order to move the field forward. To further understand the biomechanics of age-related changes in gait function, research should include multidisciplinary studies of the mechanisms of altered gait as we age. To identify the mechanisms of these alterations, physiologically relevant *in vivo*, *in vitro*, and *in silico* studies of the neural, body composition, bioenergetic, and musculoskeletal factors that support human gait should be conducted. Likewise, tendon and extracellular matrix changes are an understudied area that may provide key information about the mechanisms of age-related changes to mobility. To harness the power of wearable sensors, collaboration with behavioral and data scientists will be important for successful study designs, appropriate interpretation of the data, and overall exploration and management of rich data sets. Exoskeleton technologies are in development that may operate in assistance or resistance modes during locomotion; future studies should investigate how and when to deliver these devices to older adults. Finally, to address all aspects of the problem, inclusive studies of diverse sectors of the population are needed, and creation of common core measurements and data-sharing mechanisms should be explored. Gait is fundamental to mobility, and mobility is essential to optimize health. The study of the causes and consequences of age-related changes in mobility is an untapped opportunity for scientists and clinical gerontologists to improve the mobility, health and quality of life of our aging population.

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