

Aging, Body Composition, and Cognitive Decline: Shared and Unique Characteristics

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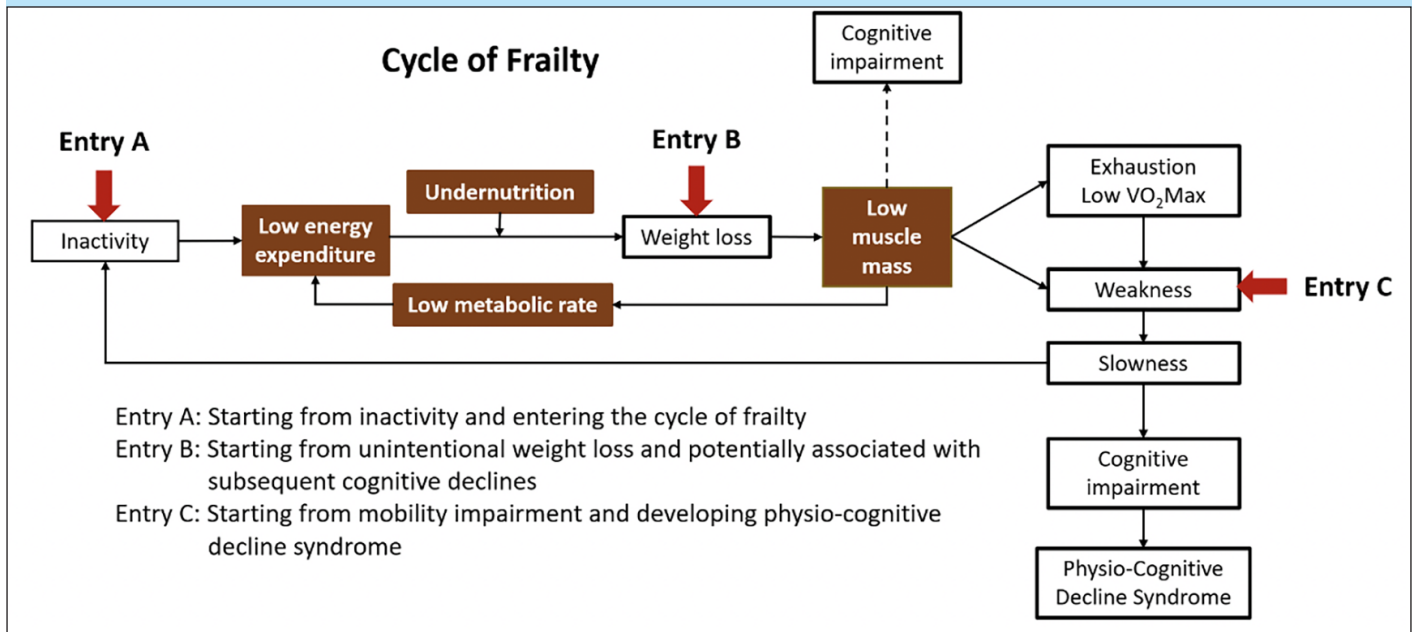
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Aging is a complex process that is intertwined with the disruption of homeostasis, the diminution of physiological reserves, the deterioration of organ function, an increased predisposition to morbidity or multimorbidity, and heightened susceptibility to social vulnerability, all of which collectively contribute to unfavorable outcomes. Among the myriad physiological alterations associated with aging, changes in body composition may represent the most significant age-related phenotypic manifestations (1). These age-related changes in body composition not only have inherent pathological implications, such as osteoporosis, obesity, and sarcopenia, but also serve as predictors for other diseases, such as cardiovascular disease and dementia. In a recent study, Uchida et al. used data from a longitudinal cohort and found that decreased fat-free mass and muscle mass over a 6-year period were associated with faster declines in global cognition over the subsequent 4 years in older men (2). The question of whether the sole loss of muscle mass is a sufficient predictor for subsequent cognitive decline remains an intriguing area of inquiry in scientific research. Recently, a review posits that physical inactivity in older adults leads to dysfunctional myokine secretion, which in turn may cause cognitive impairment and dementia due to systemic inflammation, impaired muscle glucose metabolism, deficient brain protein metabolism, and increased oxidative stress from dysfunctional mitochondria (3). However, it has been demonstrated that dynapenia, i.e., weakness or slowness, is a more significant determinant for cognitive declines than low muscle mass alone (4). It has been revealed that robust older adults may progressively transition into subtypes of frailty – mobility and non-mobility frailty (5). Notably, a decline in cognitive performance was observed following the onset of mobility frailty. Specifically, the observed decline in cognitive performance was predominantly in verbal fluency and executive function. This finding aligns with other studies, that cognitive impairment associated with mobility impairment primarily affects non-memory domains (6).

An intriguing point of discussion is the sex-specific association between muscle loss and cognitive decline in the aging process. Previous research has indicated that

Asian women do not typically experience muscle loss over time from middle age, unlike Asian men or Caucasians (7). A declining trend of muscle mass in women has been reported in Hong Kong, but it was only observed in women over the age of 80 (8). Asian people tend to have a significantly higher percentage of body fat compared to Westerners across various obesity statuses, even in underweight populations (9), but this uniqueness in Asian populations may not be solely explained by the higher dietary intake of carbohydrates (10). A Korean study found nutrient intakes related to muscle loss in men only (11), while another study showed that low muscle mass is associated with a reduced likelihood of metabolic syndrome in both Australian and Korean populations, but this relationship changes when considering body fat (12). Although Asian women do not experience a significant loss of muscle mass during the aging process, there is a notable decline in both muscle strength and physical performance over time (13). A nationally representative study in Korea demonstrated that the beneficial effects of a healthy diet and lifestyle on the preservation of muscle mass were observed exclusively in women (14). Empirical evidence indicates a significant divergence in the correlation between serum myostatin levels and muscle mass among different genders. Specifically, a negative correlation is discernible solely in older males (15). While sex-different relationships between aging and muscle loss may be partly explained by the hormonal changes, but hormonal changes alone may not account for the differences in muscle loss between women with different ethnic backgrounds. Based on evidence, it's hypothesized that Asian women, due to healthier lifestyle and dietary habits, may preserve muscle mass more effectively than men.

Research suggests that a polymorphism in the IGF1 gene, associated with body composition variations, is particularly evident in older African American females, but not in younger ones (16). A recent study found that serum IGF-1 levels were exclusively correlated with muscle mass in older men, not women, leaving the roles of IGF-1 and its genetic polymorphism in relation to muscle mass in women still unclear (17). While studies have established that body composition varies between genders, the rates of muscle mass decline differentiated by sex and ethnicity are unknown. However, it is important to note that beyond inherent genetic or biological factors, lifestyle elements influenced by sociocultural contexts may have a more substantial impact and deserve more studies.

Figure 1. Cycle frailty and potential entry for subsequent cognitive impairment

In the widely accepted «cycle of frailty» concept, individuals can enter the cycle through any of its five components (inactivity, weight loss, weakness, slowness, and exhaustion), leading to gradual deterioration (Figure 1) (18). Traditionally, inactivity is often observed as the initiator in the development of frailty, supported by a latent class analysis for physical frailty (Entry A of Figure 1) (19). However, when considering cognitive impairment in the progression of frailty, a consensus linking the process of frailty development and subsequent cognitive impairment is yet to be established, despite significant associations between them. Uchida et al.'s study suggests that weight loss alone may precede cognitive impairment (Entry B of Figure 1). A prior study has indicated that atrophic myotubes secrete exosomal miRNA into the circulation, specifically miR-29b-3p, which accelerates neuronal senescence (20). This observation may resonate with the primary findings of Uchida et al.'s work. Besides, weakness and/or slowness has been identified as early indicators of the physio-cognitive decline syndrome (PCDS) that subsequently results in disability, dementia, and mortality (Entry C of Figure 1) (21, 22). In PCDS, atrophy of grey matter volume in the cerebellum, basal ganglia, hippocampus, and amygdala linked by the cerebello-limbic neurocircuit may represent a unique entity in the development of cognitive impairment within the context of physical frailty (23). As previously mentioned, aging is a complex process that involves numerous factors and diverse developmental trajectories, but leading to common adverse outcomes such as disability, dementia, or mortality. Nonetheless, distinct traits may exist, and the muscle mass loss alone could provide a novel avenue for research into sex- and ethnicity-specific presentations, particularly the role of myokines in pathophysiology and muscle-to-brain axis to healthy aging.

Conflict of interest: The author declares no conflict of interest.

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