v. 4, n. 11, 2024

International Journal of Health Science

SARCOPENIA AND COGNITIVE DECLINE IN THE ELDERLY: A LITERATURE REVIEW TAILORING THE MUSCLE-BRAIN AXIS

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Abstract: Objective: Investigate the possible relationship between sarcopenia and cognitive decline in the elderly. **Methods:** Narrative bibliographic review in the PubMed database using the search strategy: (sarcopenia) AND (cognitive) AND (elderly). From this search, 476 articles were found, subsequently submitted to the selection criteria, selecting a total of 21 articles to compose the present study. **Discussion:** It is clear that patients with sarcopenia have a doubled risk of cognitive impairment. This correlation is independent of ethnicity and shares several pathophysiological mechanisms, such as hypoperfusion in brain areas such as the anterior cingulate cortex and the left insula. Risk factors for this relationship include advanced age, obesity, low education level, smoking, low albumin levels, vitamin D deficiency, and malnutrition. Furthermore, the role of oxidative stress, inflammatory factors such as interleukin-6, and the balance between muscle protein synthesis and muscle protein levels in the etiology of sarcopenia is highlighted. The importance of preventing cognitive impairment through increasing muscle mass, nutritional therapy and physical training to delay cognitive impairment in patients with sarcopenia is emphasized. **Final considerations:** Research shows that sarcopenia and cognitive decline in the elderly are related, sharing pathophysiological mechanisms such as cerebral hypoperfusion, which affects important areas such as the amygdala and hippocampus. However, the need for more clinical research is highlighted to deeply explore the mechanisms involved in this relationship.

Keywords: Sarcopenia, Cognitive Decline, Muscle-Brain Axis.

INTRODUCTION

Sarcopenia and cognitive decline manifest themselves as conditions intrinsic to the aging process, exerting a substantial influence on mortality and quality of life in the elderly. These conditions predispose affected individuals to a high risk of falls, disabilities in daily activities and compromised mental health (BASILE G; SARDELLA A., 2020) (YUENYONGCHAIWAT, K.; BOONSINSUKH, R., 2021). The phenomena of sarcopenia and cognitive decline are widely investigated in gerontology, considering their correlation with morbidity and mortality in the elderly.

The bidirectional interaction between sarcopenia and cognitive decline suggests a reciprocal influence between these conditions, where sarcopenia can accentuate cognitive decline and vice versa (BASILE G; SARDELLA A., 2020). The association between sarcopenia and cognitive impairment has been evidenced in studies who demonstrated that elderly people with reduced muscle strength are at greater risk of cognitive problems, highlighting a doubled risk of cognitive impairment and dementia in sarcopenic patients (PENG TC et al., 2020).

This article aims to investigate the interrelationship between sarcopenia and cognitive decline in the elderly, exploring the contribution of physical activity as a protective factor. The release of myokines during muscle contraction, induced by physical exercise, emerges as a promising mechanism in mediating muscle-brain communication, potentially attenuating the effects of sarcopenia and promoting improved cognitive function. Recent studies highlight the importance of myokines in improving physical fitness, gaining muscle mass, and promoting increased activity in brain regions associated with memory and cognition, such as the prefrontal cortex and hippocampus (AROSIO B. et al., 2023) (HAN X. et. al., 2023).

METHODOLOGY

This is a narrative bibliographic review developed in accordance with the criteria of the PVO strategy, an acronym that represents: population or research problem, variables and outcome, used to prepare the research through its guiding question: "Is there a relationship between sarcopenia and cognitive decline in the elderly, and how can the mechanisms of the muscle-brain axis influence this relationship?" In this sense, according to the parameters mentioned above, the population or problem of this research refers to elderly patients who present sarcopenia in order to investigate the relationship between sarcopenia and cognitive decline focusing on the biological, hormonal and neurological mechanisms that connect the muscle to the brain with the purpose of improving the quality of life of these patients. The searches were carried out by searching the PubMed Central (PMC) database. The search terms were used in combination with the Boolean term "AND" through the search strategy: (sarcopenia) AND (cognitive) AND (elderly). From this search, 476 articles were found, subsequently submitted to the selection criteria. The inclusion criteria were: articles in the English language published between 2019 and 2023 and that addressed the themes proposed for this research, studies of the review and meta-analysis type, available in full. The exclusion criteria were: duplicate articles, available in abstract form, which did not directly address the proposal studied and which did not meet the other inclusion criteria. A total of 21 articles were selected to compose the present study.

DISCUSSION

The correlation between sarcopenia and cognitive impairment is notable, evidenced by the fact that patients with sarcopenia have a doubled risk of cognitive impairment, with this correlation being independent of ethnicity (PENG TC et al., 2020). Another significant aspect of this correlation is that some patients undergoing neurological tests to identify cognitive changes were also diagnosed with excessive muscle loss (FHON JRS et al., 2023). Although it is not fully elucidated, there are some explanations that can help understand the association between sarcopenia and cognitive decline (BAI A. et al., 2021). This occurs because the loss of skeletal muscle mass and cognitive disorders share many pathophysiological mechanisms in common, which led researchers to investigate the relationship between the two (YIGIT B. et al., 2022). In an analytical study using mapping software, it was found that participants with sarcopenia (n = 56) presented hypoperfusion in the bilateral anterior cingulate cortex and left insula, compared to those without sarcopenia (n = 39). Furthermore, other areas of the brain showed hypoperfusion, with atrophy observed in the main limbic centers, amygdala and hippocampus, corroborating the prevalent association between cognitive deficit and sarcopenia (DEMURA T. et al., 2022).

When addressing the main risk factors associated with the relationship between sarcopenia and cognitive decline in the elderly, Cipolli et al. (2023) states that patients with sarcopenia are, for the most part, older, obese, with a lower level of education and smokers. Furthermore, sarcopenia, after 10 years of follow-up, was associated with the occurrence of low cognitive performance, with verbal fluency being the main affected parameter. Furthermore, Xiaolei L. et al. (2021) attributed a greater risk to patients who had low albumin levels, vitamin D deficiency and malnutrition, which increased the risk of sarcopenia thirteen times. They also showed that individuals with poor sleep quality showed increased muscle degradation, as they have lower levels of IGF-1 and higher levels of cortisol, a catabolic hormone. According to Peng TC et al. (2023), hormonal and inflammatory markers are associated with cognitive impairment and sarcopenia; therefore, the pillars for preventing the disease involve reducing inflammation, minimizing brain damage and increasing cognitive reserve, these three factors being closely associated with muscles and physical activity.

Sarcopenia is mainly due to low muscle strength. The balance between muscle protein synthesis and muscle protein levels may be a major contributor to the etiology of muscle atrophy in patients with sarcopenia (YANG Y. et al., 2022). According to Szlejf C. et al. (2019), low muscle strength was associated with worse performance across all cognitive domains and may drive the association between sarcopenia and cognition. It is clear that the inflammatory process and oxidative stress play a pathological role in both conditions (BAI A. et al., 2021).

According to Lin A. et al. (2023), oxidative stress, tumor necrosis factor and inflammation with a predominance of interleukin-6 are shared factors for sarcopenia and cognitive decline. Associated with this, there is an influence of changes in the circulating level of myokines, as these have an important role in cognition and are produced by skeletal muscle. Furthermore, according to Merchant et al. (2023), dementia, predominant in sarcopenic individuals, can accelerate weakness. It has been demonstrated that patients with motor cognitive risk have a higher prevalence of depression, in addition to impairment in activities of daily living.

Excess oxidative stress, related to chronic diseases, can cause loss of skeletal muscle

mass and, consequently, sarcopenia (CIPOLLI GC et al., 2021). Furthermore, age-related inflammation, which is characterized by elevated levels of interleukin-6 and necrosis factor-α, has been reported as a possible important cause of both sarcopenia and lower cognitive performance (CIPOLLI GC et al., 2021). According to Bai A. et al. (2021), elevated concentrations of inflammatory markers have been implicated in mobility impairment, as well as being a marker of new-onset dementia. Obesity has been postulated as a possible cause of chronic low-grade inflammation (MANGGE et al., 2014; WOODS et al., 2012; YUDKIN, 2007), associated with neuroinflammation in the hypothalamus, hippocampus, amygdala, cerebral cortex and cerebellum in models diet-induced obesity animals (BEILHARTZ et al., 2016; GUILLEMOT-LEGRIS et al., 2016; LU et al., 2011;TAPIA-GONZALEZ et al., 2011) and in the occipitoparietal cortex in a human H-MRS study (GONZALEZ et al., 2012). It is concluded, then, that a healthy percentage of fat and muscle strength are associated with correlates of brain health, measured as greater brain volumes or neural integrity (VINTS WAJ et al., 2023). Therefore, for Maniscaldo et al. (2023), the prevention of cognitive impairment is imperative, considering that there is still no known way to cure dementia. Therefore, Amini et al. (2023) concluded that increasing muscle mass is a key intervention in preventing cognitive decline. Therefore, nutritional therapy and physical training must be encouraged in patients with sarcopenia to delay global cognitive impairment.

FINAL CONSIDERATIONS

This study contributes significantly to the understanding of the relationship between sarcopenia and cognitive decline in the elderly, a field of research that is increasingly highlighted due to the pathophysiological interconnections between these two conditions. Sarcopenia, characterized by progressive loss of skeletal muscle mass and strength, and cognitive decline are prevalent phenomena in the elderly population and share several underlying biological mechanisms. A direct relationship between sarcopenia and cognitive decline was evidenced, significantly influenced by the muscle-brain axis. Specifically, it was observed that hypoperfusion in critical areas of the brain, such as the hippocampus and amygdala - important centers for memory and cognitive function - is associated with muscular atrophy and, therefore, sarcopenia. This finding suggests that cognitive deterioration in the elderly may reflect broader neuromuscular changes. However, there is still an urgent need for further clinical research to fully unravel the pathophysiological mechanisms that link sarcopenia and cognitive decline. A more detailed understanding of these mechanisms may pave the way for more effective interventions in both prevention and treatment of these conditions in older adults. Furthermore, it is essential to consider the influence of factors such as nutrition, physical activity, and comorbidities on the development and progression of sarcopenia and cognitive decline. This study highlights the importance of a multidisciplinary approach to understanding the complexity of the relationship between sarcopenia and cognitive decline, emphasizing the need for intervention strategies that address both the physical and cognitive health of older adults. Recognizing and effectively treating sarcopenia can have significant implications for the preservation of cognitive function and, consequently, for quality of life in old age.

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