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REVIEW

Imaging Biomarkers of Cognitive Impairment in Sarcopenia: A Narrative Review

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Abstract: Sarcopenia is characterized by progressive declines in muscle strength, mass, and physical function. Mild cognitive impairment (MCI), also referred to as mild neurocognitive disorder (mNCD), involves a measurable reduction in cognitive abilities that does not substantially interfere with daily independence, thereby distinguishing it from dementia. With global population aging, both conditions have emerged as prevalent health concerns, and understanding cognitive status among individuals with sarcopenia has become increasingly important. This narrative review synthesizes current neuroimaging findings related to cognitive impairment in sarcopenia, examining both the mechanistic underpinnings and clinical relevance of this association. Particular emphasis is placed on the Muscle-Brain Axis, which provides a foundational framework for understanding how imaging biomarkers may bridge sarcopenia and cognitive decline. Within the imaging domain, this article focuses on Magnetic Resonance Imaging (MRI) and Positron Emission Tomography (PET), reviewing their applications in detecting and characterizing cognitive impairment among patients with sarcopenia.

Keywords: sarcopenia, cognitive impairment, magnetic resonance imaging, positron emission tomography, muscle-brain axis

Introduction

The European Working Group on Sarcopenia in Older People (EWGSOP) proposed three diagnostic criteria for sarcopenia, based on muscle mass, muscle strength, and physical performance.[1] While sarcopenia is commonly recognized for its physical impacts, such as reduced mobility and a higher risk of falls, emerging studies have also identified a potential link between this condition and cognitive decline.[2] Among individuals aged 60 years and older with sarcopenia, the prevalence of cognitive impairment has been reported to vary between 9.9% and 40.4%.[3] However, several important knowledge gaps remain. First, the neurobiological mechanisms linking sarcopenia to cognitive impairment are not fully understood. Second, although various neuroimaging techniques have been used to investigate cognitive changes in sarcopenia, the specific imaging features that characterize sarcopenia-related cognitive impairment have not been systematically synthesized. Addressing these gaps is essential for advancing both mechanistic understanding and clinical practice. A previous meta-analysis found that older adults with sarcopenia have a two-fold higher risk of cognitive decline.[4] Furthermore, individuals with sarcopenia-especially those with coexisting cognitive impairment or comorbidities-were found to have the highest risk of mortality from chronic cerebrovascular diseases (CCVDs) and Alzheimer's disease (AD).[5] While neuropsychological tests such as the Mini-Mental State Examination (MMSE) and Montreal Cognitive Assessment (MoCA) are widely used to screen for cognitive impairment, these instruments provide only a global summary of cognitive performance. They do not reveal the underlying structural or molecular brain changes that may mediate the relationship between sarcopenia and cognitive decline. Consequently, traditional cognitive assessments alone are insufficient to elucidate the pathophysiological mechanisms linking muscle deterioration to brain

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dysfunction. Therefore, Non-invasive and holistic detection of cognitive impairment in the context of sarcopenia is therefore of critical clinical importance.

Given the growing body of research on cognitive impairment in sarcopenia, the role of imaging in diagnosing this condition warrants further investigation. Cognitive impairment in older adults arises from complex neuropathological changes. In the context of sarcopenia, the accumulation of cerebral Aβ and alterations in both gray and white matter may serve as key dynamic factors contributing to this decline.[6] Examining the link between muscle mass and neuroimaging biomarkers, including cortical thickness, hippocampal volume, predicted brain age, and markers of small vessel disease, may offer critical insights into body-brain interactions that affect susceptibility to cognitive disorders.[7] These insights can be valuable for diagnosing and improving the prognosis of cognitive impairment in the context of sarcopenia and are summarized in the following sections.

Therefore, this review has two specific objectives: (1) to summarize the neuroimaging findings associated with cognitive impairment in sarcopenia; and (2) to discuss the potential pathophysiological mechanisms linking sarcopenia to cognitive decline, with emphasis on the muscle-brain axis.

Search Strategy

A literature search was conducted using PubMed and Web of Science databases up to March 2026. Search terms included combinations of "sarcopenia", "cognitive impairment", "mild cognitive impairment", "neuroimaging", "MRI", "PET", "white matter hyperintensities", and "hippocampus". Inclusion criteria were: (1) original research articles or reviews; (2) studies involving human participants; (3) studies reporting neuroimaging findings in relation to sarcopenia or cognitive impairment. Exclusion criteria were: (1) non-English articles; (2) conference abstracts; (3) animal studies. The initial search yielded approximately 500 articles, which were screened by title and abstract, and 102 relevant references were ultimately cited in this review. Given the limited number of studies directly examining neuroimaging in sarcopenic patients with cognitive impairment, the review also includes studies on MCI and AD in general populations, with extrapolation to sarcopenia explicitly noted where applicable. This narrative review was reported with reference to the SANRA (Scale for the Assessment of Narrative Review Articles) guidelines.

Elaborate on the Muscle-Brain Axis in the Context of Sarcopenia and Cognitive Impairment

Accumulating evidence underscores a robust bidirectional interaction between cognitive and motor systems in shaping physical function.[8] The Muscle-Brain Axis encapsulates a bidirectional relationship wherein sarcopenia contributes to cognitive decline, while neurological factors underlying cognitive impairment also participate in the pathophysiology of sarcopenia. Elucidating this reciprocal interaction is therefore of considerable importance.[9]

Molecular Mechanisms of Neural Factors Affecting Sarcopenia

Neuromuscular junctions (NMJs) constitute the critical connection point linking motor neurons with skeletal myofibers. While their architecture resembles that of typical chemical synapses, consistent activation of these junctions is fundamental to sustaining muscle mass and functional capacity.[9] Evidence indicates that NMJs are a key factor in the pathogenesis of age-related musculoskeletal decline, including conditions such as sarcopenia.[10,11] Adequate physical performance relies on the precise coordination and communication between the nervous and muscular systems, a process that is both intricate and highly regulated.[9] Movement coordination by the brain begins when upper motor neurons in the motor cortex generate action potential that transmit signals to lower motor neurons in the posterior spinal cord. From there, the impulse travels along the axon of the motor neuron to reach the NMJs.[9] Age-related deterioration of NMJs manifests through both morphological and functional changes. These include disrupted organization of pre- and postsynaptic membranes, diminished numbers of neurotransmitter-laden synaptic vesicles, and impaired axonal transport velocity.[12] NMJs deterioration and other imbalance may act synergistically to induce age-related muscle decline which is an important mechanism causing sarcopenia.[9]

Targeting the Brain-Muscle Axis: The Impact of Sarcopenia on Cognitive Impairment

A growing body of evidence points to a bidirectional association between sarcopenia and cognitive function. Neurological processes not only affect muscle integrity but also, conversely, the advancement of sarcopenia appears to exert deleterious effects on cognitive performance.[9] Research shows that mitochondrial dysfunction has been associated with muscle aging which is closely related to sarcopenia.[13] Mitochondrial dysfunction, manifesting as impaired metabolism, disrupted respiration, altered dynamics, redox imbalance, dysregulated ion homeostasis, and abnormal cell death signaling, represents a central pathogenic mechanism across most neurodegenerative conditions, including cognitive impairment.[14,15] Emerging evidence suggests that mitochondrial dysfunction in skeletal muscle, a key feature of sarcopenia, may represent an upstream event linking muscle deterioration to cognitive decline. This relationship appears to be mediated, at least in part, by increased muscle fat infiltration, which has been associated with accelerated brain aging and reduced psychomotor speed.[16] Therefore, mitochondria probably play an important mediating role in the impact of sarcopenia on cognitive impairment.

Mitochondria contribute to muscle-brain crosstalk via two potential mechanisms: first, through the release of circulating factors such as myokines, which often require mitochondrial function for their secretion; and second, possibly through the direct transfer of mitochondria from muscle cells to other tissues.[17] In fact, contracting muscle fibers produce and release myokines,[18] multiple lines of investigation have demonstrated that exercise-stimulated myokine secretion serves as a key signaling mechanism in the bidirectional communication between skeletal muscle and the brain.[19,20] The physiological impact of myokine release is governed by key exercise parameters, including duration, intensity, and frequency, which collectively shape their functional outcomes.[21] The term "myokineome" has been coined to describe the repertoire of myokines secreted in response to exercise, which includes irisin, cathepsin B, fibroblast growth factor 21 (FGF-21), BDNF, and numerous others.[22] While these myokines collectively contribute to systemic exercise-related signaling, several have been specifically implicated in central nervous system effects. This suggests that they may function, at least in part, as mediators of the cognitive benefits associated with regular physical activity.[17] The beneficial effects of exercise on cognition in aging populations may be mediated, at least in part, by myokine signaling. This is supported by observed increases in activity within the prefrontal cortex and hippocampus, both critical for memory and cognitive processing.[23–27] Contracting skeletal muscle secretes myokines that influence hippocampal function through both direct pathways and indirect modulation of BDNF levels. Growing evidence implicates cathepsin B as a key mediator: elevated peripherally by exercise, this myokine crosses the blood-brain barrier and stimulates BDNF production, thereby promoting neurogenesis and enhancing memory and learning.[28] Conversely, a detrimental effect of a physically inactive lifestyle and sarcopenia which have long been established will be found. A sedentary lifestyle disrupts normal myokine synthesis and secretion, thereby contributing to cognitive impairment and promoting neurodegenerative processes.[9] A large-scale UK Biobank study revealed that sensorimotor brain regions play a mediating role in the relationship between sarcopenic and cognitive traits. The same investigation further demonstrated that regional brain structure serves as a mediator linking these two domains[29] (Figure 1). Therefore, in-depth study on cognitive impairment in the context of sarcopenia has become essential.

Clinical Comorbidity of Sarcopenia and Cognitive Impairment

Compared with patients without sarcopenia, patients with sarcopenia had a greater probability of suffering from mild cognitive impairment and dementia,[4] which indicates that sarcopenia is independently associated with cognitive impairment.[5] Sarcopenia and cognitive impairment overlap in their underlying risk profiles, sharing common predisposing conditions such as cerebrovascular disease, diabetes, and hypertension.[30–32] Relative to cognitively intact individuals, those with mild cognitive impairment (MCI) were characterized by older age, male predominance, lower educational attainment, and a higher prevalence of diabetes in their medical history.[30] Sarcopenia was also further associated with a high risk of diabetes, hypertension among general populations.[33] In addition, the chronic inflammatory state resulting from immune senescence and the increased secretion of cytokines may lead to adverse outcomes.[34] Elevated circulating levels of interleukin-6 (IL-6) and C-reactive protein (CRP) have been linked to the progressive loss of skeletal muscle

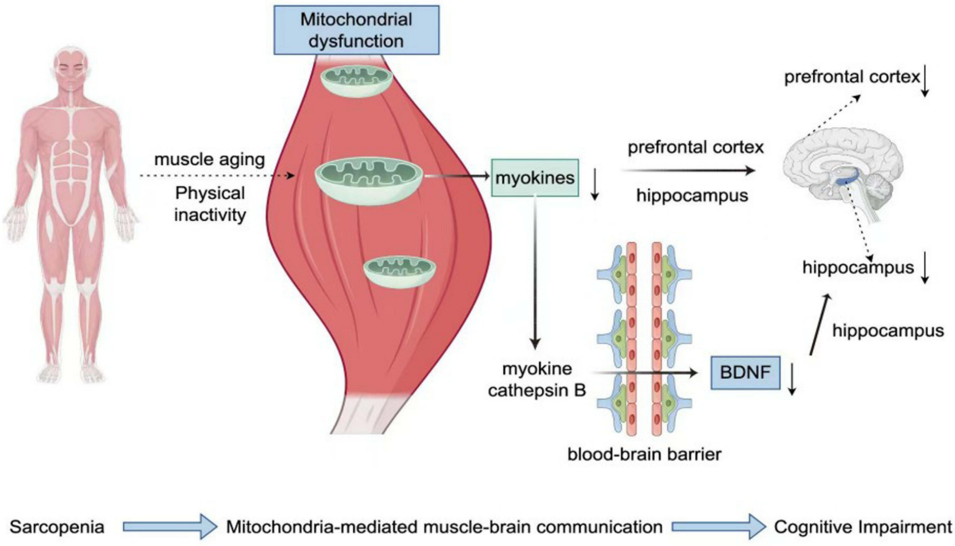

Figure 1 The process by which sarcopenia induces cognitive impairment. Mitochondrial dysfunction as a potential mediator in the muscle-brain axis linking sarcopenia to cognitive impairment. Impaired mitochondrial function in skeletal muscle may contribute to muscle fat infiltration and systemic metabolic disturbances. These abnormalities may in turn affect brain regions critical for cognitive function, including the hippocampus and prefrontal cortex, through myokine signaling pathways. This suggests a common pathogenic pathway connecting muscle deterioration to cognitive decline. (Created with figdraw.com).
Abbreviation: BDNF, brain-derived neurotrophic factor.

mass[35] and muscle strength[36] and an increased risk of dementia.[37] Lower serum testosterone levels are associated with lower muscle mass and strength[38] and are independent predictors of dementia.[39]

Sarcopenia is fundamentally driven by the loss of muscle strength. Compounding this, physical inactivity and suboptimal rehabilitation strategies can further curtail overall activity levels, thereby exacerbating the condition.[34] A well-established body of literature demonstrates that physical activity plays a crucial role in both enhancing cognitive function and maintaining cognitive stability over time.[40] A meta-analysis pooling 15 prospective cohort studies with 33,816 initially dementia-free participants revealed that higher physical activity levels confer significant protection against the subsequent development of dementia. The protective effect was most pronounced among those engaging in the highest levels of activity.[41] Therefore, physical activity is beneficial for improving the prognosis of sarcopenia and cognitive impairment as well as preventing their onset, and it also serves as an important direction for researching the relationship. Taken together, the above findings suggest that sarcopenia is associated with an increased risk of cognitive impairment.[42–45] (Table 1).

Imaging of Cognitive Impairment in the Context of Sarcopenia

Recent evidence indicates that sarcopenia serves as a predictor for the development of mild cognitive impairment (MCI) and Alzheimer-type dementia (DAT).[46,47] Modern imaging techniques such as PET and MRI offer the capability to detect molecular-level pathology in individuals with MCI[48] and these imaging detection tools are also of great significance to the study of cognitive impairment in the context of sarcopenia. The advent of neuroimaging has enabled the detection of structural and functional brain alterations, permitting unprecedented insights into in vivo brain changes.[49] A growing body of neuroimaging evidence has linked cognitive impairment to a spectrum of underlying pathological events. These include molecular abnormalities such as ß-amyloid and tau protein deposition, structural changes like gray matter atrophy and white matter disruption, and functional deficits in brain activity[50–52] (Figure 2).

MRI

Structural MRI

White matter hyperintensities (WMH), frequently observed on structural MRI in patients with Alzheimer's disease, are well established as a risk factor for cognitive decline.[53,54] WMH have been linked to physical frailty, manifesting as

Table 1 Different Imaging Detection Tools Application in Diagnosing the Cognitive Impairment in the Context of Sarcopenia

Clinical Application	References	Study Size	Acquisition	Modeling Method	Results	Clinical Score Scale	Evidence Type
Establishing diagnosis	Sunghwan Kim et al[6]	528	FLAIR MRI images and amyloid PET images	Propensity Score Matching	Global cognitive function correlated with all sarcopenia components; however, cortical thickness and Aβ retention displayed differential relationships across these measures	Clinical Dementia Rating (CDR) and Mini-Mental State Examination (MMSE)	Direct
Development and prevention of cognitive impairment	Tiril P. Gurholt et al[29]	33709	Whole-body MRI	Multiple Linear Regression	Sarcopenic traits correlate with lower cognitive function and multiple brain MRI measures	Not reported	Extrapolated
Preventing cognitive impairment	Kangrui Zhang et al[42]	95	A 1.5T superconducting MRI machine	Multiple Linear Regression	Lower scores on sarcopenia measures were significantly linked to cognitive decline	Montreal Cognitive Assessment (MoCA)	Direct
To evaluate whether current sarcopenia definitions relate to cognition in older community-dwelling women	Abellan van Kan G et al[43]	3025	Dual energy X-ray absorptiometry	Multivariate logistic regression	No sarcopenia definition predicted cognitive impairment after confounder adjustment	Short portable mental status questionnaire	Extrapolated
This study examined the sarcopenia-sleep relationship in female mild-to-moderate AD patients	Shanwen Liu et al[44]	112	MMSE and MoCA	Binary logistic regression	Female sarcopenia patients have more sleep symptoms and cognitive impairment	Sleep quality was measured using the PSQI, and cognitive performance was evaluated via the MMSE and MoCA.	Extrapolated
To investigate sarcopenia-cognition association and examine long-term prognosis	Chong Zhang et al[5]	2890	Data from NHANES	Multivariable logistic regression	The coexistence of sarcopenia with cognitive impairment or comorbidities in older adults is associated with higher mortality from CCVDs and AD relative to healthy individuals	Cognitive assessment comprised three standardized instruments: the CERAD Word Learning subtest for verbal memory, the Animal Fluency Test for semantic fluency, and the Digit Symbol Substitution Test for processing speed	Extrapolated
To assess whether muscle strength relates to cognition and MTA in mild-to-moderate AD	S W Liu et al[45]	80	3.0T coronal three-dimensional gradient echo sequence MRI	Partial correlation analysis	Compared to muscle mass and physical function, decreased muscle strength is significantly associated with widespread cognitive decline and increased degree of medial temporal lobe atrophy	Neuropsychological assessment included measures of global cognition (MMSE, MoCA), memory and executive function (MES, VFT), and attention/processing speed (DSST, DST)	Extrapolated

reduced gait speed and diminished hand grip strength.[2,55] A study found that total WMH and Paraventricular Hypothalamic Nucleus(PVH) volumes in patients with cognitive impairment were significantly associated with gait speed and 5-STS (Sit-to-Stand) time, even after adjusting for confounding factors.[56] An additional study revealed that, compared to normal controls, the AD group exhibited significantly greater WMH volume as well as a higher prevalence of sarcopenia.[56] In patients with Alzheimer's disease, WMH volumes were found to correlate with performance across multiple cognitive domains. Notably, periventricular hyperintensity (PVH) volume demonstrated a moderate association with executive dysfunction.[56] Moreover, sarcopenic parameters, including gait speed and 5-STS time, were significantly associated with WMH volumes.[56] Further evidence from a cross-sectional study of memory clinic patients revealed that white matter hyperintensities were linked to deficits in both gait speed and chair stand performance.[57] These findings suggest that changes in WMH volume may not only help identify cognitive impairment but also indicate a potentially higher risk of sarcopenia.

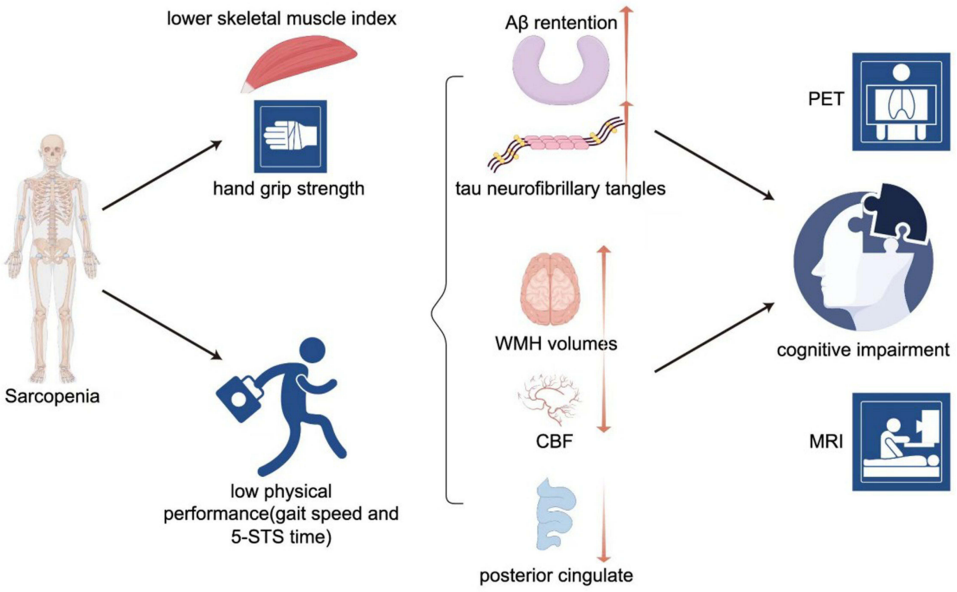

Figure 2 Detection of imaging biomarkers in the context of sarcopenia. Common brain changes seen on MRI and PET in patients with cognitive impairment. These include white matter hyperintensities (WMH), increased tau neurofibrillary tangles and Aβ retention, reduced cerebral blood flow (CBF), and posterior cingulate atrophy. (Created with figdraw.com).

Leukoaraiosis refers to cerebral subcortical white matter changes visible as decreased density on CT or hyperintensities on T2-weighted MRI. These alterations are accompanied by diffusion abnormalities in both hyperintense and normal-appearing white matter, and represent a common finding in elderly individuals, irrespective of whether cognition is normal, mildly impaired, or demented.[58] Among various neuroimaging measures, cortical gray matter fractal dimension (FD) emerged as the most significant predictor of cognitive decline, according to findings from a recent investigation.[59] Importantly, fractal dimension (FD) can be obtained from standard high-resolution 3D T1-weighted images that are routinely acquired in clinical MRI protocols, enhancing its translational potential. More recently, machine learning algorithms have been developed to predict conversion from MCI to Alzheimer's disease using longitudinal whole-brain 3D MRI data.[60] Together, conventional WMH assessment and emerging approaches such as FD and machine learning may offer complementary tools for future longitudinal studies investigating the relationship between sarcopenia and cognitive impairment. In summary, structural MRI reveals that white matter hyperintensities and gray matter changes are associated with both cognitive decline and sarcopenia risk, suggesting that WMH may serve as a shared imaging marker linking these two conditions.

Diffusion MRI

Cognitive decline observed in healthy aging as well as age-related disorders is associated with cortical "disconnection". This disconnection is primarily due to white matter damage, which in turn leads to a reduction in functional integration among distant cortical regions.[61] Diffusion MRI (DMRI) enables in vivo assessment of white matter microstructure and properties. Its diffusion metrics sensitively capture structural abnormalities associated with axonal injury or demyelination. Notably, DMRI indices derived from normal-appearing white matter demonstrate stronger correlations with cognitive performance than conventional MRI markers.[62]

Diffusion tensor imaging (DTI) studies have recently revealed that both gray and white matter undergo pathological changes in MCI and AD, with consequential disruption of hippocampal connectivity,[63] posterior cingulum,[63,64] thalamus[65] and extend to posterior white matter regions, with these alterations also correlating with the severity of cognitive impairment.[66] Moderate physical activity performed in midlife or late life was associated with hippocampal volume which is a reduced risk of MCI.[66,67] Considering that the hippocampus is also a key brain region responsive to myokine signaling and physical activity, as discussed in the context of the muscle-brain axis, the hippocampus may serve as a starting point for establishing the muscle–brain–imaging axis and holds important research significance. The primary

metrics derived from DTI include mean diffusivity (MD), which quantifies the average rate of water molecule diffusion, and fractional anisotropy (FA), which reflects the directional variability of diffusion.[68] Widespread microstructural disruptions, evidenced by reduced FA and elevated MD in regions such as the cingulum bundles and corpus callosum, along with marked topological changes in the structural connectome, have been consistently reported in Alzheimer's disease.[49] While both MCI and AD patients exhibit white matter microstructural disruptions, a key distinction lies in the spatial extent of FA abnormalities. Specifically, FA reductions in AD extend to occipital and parietal regions, whereas MCI patients show relative preservation of FA in these areas.[69] However, it remains unclear whether sarcopenia accelerates this progression or follows a distinct spatial pattern. Furthermore, the cross-sectional design of existing studies precludes causal inferences, and longitudinal studies are needed to determine whether sarcopenia-associated white matter changes precede or follow cognitive impairment. Beyond providing global summary indices, diffusion MRI offers the capability to characterize the spatial distribution of white matter alterations. Converging evidence from voxel-based and tractography approaches has pinpointed key white matter tracts whose integrity is most closely associated with cognitive performance, particularly in executive function and verbal memory.[70–72] Therefore, in-depth application of DTI to assess the hippocampus and the integrity of these white matter regions may provide valuable insights into cognitive impairment in the context of sarcopenia.

WMH, common in aging and associated with vascular risk factors, are recognized contributors to cognitive impairment. Intravoxel incoherent motion (IVIM) imaging has been employed to assess microvascular and parenchymal microstructural changes within WMH, aiming to elucidate their relationship with cognitive function.[73] Using a biexponential fitting approach, IVIM disentangles diffusion and perfusion effects by quantifying three distinct parameters: D, representing pure diffusion coefficient; D*, reflecting perfusion-related pseudo diffusion; and f, the fraction of signal attributable to the microvascular compartment.[74] A study demonstrated that IVIM parameters in the thalamus, amygdala, and hippocampus effectively distinguished between healthy controls and individuals with MCI, whereas conventional structural metrics failed to differentiate between these groups.[74] Additionally, both structural and IVIM metrics can distinguish between controls and patients with AD, as well as between MCI and AD cohorts.[74] IVIM may also distinguish cognitive impairment in the context of sarcopenia from other types of cognitive impairment and could be a useful tool for future research. In summary, diffusion MRI detects white matter microstructural disruption and hippocampal connectivity changes, which are associated with cognitive decline. The hippocampus, linking myokine signaling and physical activity, may serve as a key node in the muscle-brain-imaging axis, offering a potential biomarker for sarcopenia-related cognitive impairment.

Functional MRI

Functional MRI (fMRI) is also an important tool that greatly promotes the localization research of functional brain regions closely related to learning and memory in the context of sarcopenia. A clearcut neuropsychological profile associated with sarcopenia has not been identified so far. Nevertheless, multiple cognitive domains, including language skills, memory capabilities, and executive functions, evidently show signs of being impacted.[75–78] Functional imaging studies reveal that AD patients show reduced perfusion in the temporal lobe and in key parietal areas, including the medial (posterior cingulate cortex and precuneus) and lateral (superior and inferior parietal lobules) subdivisions,[79–81] which are compatible with the β-amyloid deposition sites.[82] Suo et al demonstrated that resistance training positively influenced the posterior cingulate cortex, an area implicated as an early biomarker in Alzheimer's disease, and also enhanced hippocampal connectivity.[83] Interventions involving coordinative and resistance training might therefore merit greater focus in research on cognitive impairment associated with sarcopenia, as this could help clarify their potential beneficial effects on brain structure and function during disease states.

Resting-state fMRI has been employed to investigate brain changes following Baduanjin exercise. Analysis of resting-state fMRI data revealed that Baduanjin practice induces frequency-specific alterations in the amplitude of low-frequency fluctuation (ALFF).[84] Specifically, Baduanjin practice significantly reduced ALFF in the right hippocampus in the classic low-frequency band, while increased ALFF was observed in the bilateral anterior cingulate cortex (ACC) in the slow-5 band.[84] Task-related fMRI investigations have consistently observed hippocampal hyperactivity during memory encoding in individuals with mild cognitive impairment (MCI).[85,86] After 24 weeks of Baduanjin training,

participants showed decreased hippocampal ALFF values alongside increased hippocampal volume when compared to the brisk walking group.[84] Furthermore, the reduction in right hippocampal ALFF correlated significantly with improvements in MoCA scores, indicating a potential link between regional brain function and cognitive enhancement following Baduanjin.[84] These neuroimaging findings suggest that Baduanjin may modulate hippocampal function and structure. However, direct evidence linking these Baduanjin-induced brain changes to sarcopenia parameters remains limited and requires further investigation.

Although research on cognitive impairment in the context of sarcopenia based on fMRI is relatively scarce, attempts can be made to establish a link between sarcopenia and cognitive impairment through physical activity and this is likely to be a worthwhile direction for fMRI research. In summary, the neuropsychological profile of sarcopenia-related cognitive impairment remains unclear based on current fMRI evidence. Nevertheless, preliminary findings suggest that physical activity (eg, Baduanjin and resistance training) may modulate hippocampal function and structure. However, direct evidence linking fMRI changes to sarcopenia parameters is still limited, and further research is needed.

Perfusion MRI

Changes in vascular factors are a crucial mechanism underlying cognitive impairment. Cerebral endothelial cell dysfunction triggers a pathological cascade beginning with impaired perfusion and blood-brain barrier (BBB) disruption. These vascular alterations subsequently contribute to brain damage, accelerate neurodegeneration, and ultimately manifest as cognitive decline.[87] According to the vascular hypothesis, cognitive impairment originates from alterations in cerebral perfusion, which in turn trigger dysfunction in neurons and their supporting cells, ultimately leading to cognitive decline.[88] Both diabetes and cardiometabolic disease can initiate reversible microvascular damage with associated dysfunction, which may eventually become irreversible and structurally apparent. The clinical consequences encompass not only classic complications such as vision loss, renal impairment, and neuropathy, but also cardiac failure and sarcopenia.[89]

Therefore, alterations in both large and small cerebral blood vessels are regarded as key factors driving cognitive impairment and vascular factors can serve as an important direction for exploring cognitive impairment in the context of sarcopenia. These changes are particularly noticeable in the white matter (WM) penetrating vasculature, though not exclusive to it.[90] Cerebral small vessel disease (CSVD) represents a leading cause of vascular cognitive impairment. Its hallmark neuroimaging features on MRI include WMHs, lacunes, cerebral microbleeds, enlarged perivascular spaces, and cerebral atrophy.[91]

A comparative study of brain structure and perfusion across MCI subtypes and healthy controls revealed both shared and distinct patterns. While both AD-MCI and subcortical vascular MCI (svMCI) exhibited decreased temporal lobe CBF, each subtype showed a unique atrophy profile: hippocampal atrophy in AD-MCI, and thalamic and postcentral gyrus atrophy in svMCI.[92] Exercise training has been shown to modulate cerebral blood flow (CBF) and enhance cognitive performance in older adults, regardless of whether they have pre-existing cognitive impairment.[93] So future studies are suggested to evaluate the mediating effects of CBF on the association between exercise training and cognition.

Emerging evidence underscores the pivotal role of cerebral hypoperfusion in the pathogenesis and progression of vascular cognitive impairment (VCI).[94] Arterial spin labeling (ASL) is a perfusion MRI technique that enables both qualitative and quantitative assessment of cerebral blood flow (CBF) without the need for exogenous contrast agents or ionizing radiation[94] and ASL is recommended for its ability to quantify subtle perfusion alterations that escape detection on structural MRI, thereby enhancing diagnostic specificity for vascular cognitive impairment (VCI).[95] A separate study employed pseudo-continuous arterial spin labeling MRI to measure cerebral blood flow (CBF) both before and after the training intervention.[96] Compared to the stretching control group, participants in the aerobic exercise (AE) group showed significant training-induced increases in CBF within the anterior cingulate cortex.[96] Moreover, the degree of memory improvement across participants correlated positively with CBF increases in the anterior cingulate and adjacent prefrontal cortices.[96] Therefore, physical activity has the potential to improve both sarcopenia and cognitive impairment by enhancing microcirculation and may become an important approach to improving cognition in the context of sarcopenia.

Positron Emission Tomography

The neuropathological hallmarks of MCI include β-amyloid (Aβ) plaques and intracellular tau neurofibrillary tangles (NFTs). PET-based molecular imaging has illuminated the complex interactions among Aβ, tau, and neuroinflammation in both AD and

MCI, helping to clarify whether these pathologies represent an extension of normal aging or a distinct disease process.[97] PET imaging has further characterized the regional distribution of neuropathological deposits and established their associations with cognitive decline, disease progression, and eventual neurodegeneration.[97] Several studies have extended these PET findings to the context of sarcopenia. Lower skeletal muscle index and reduced hand grip strength have been linked to brain atrophy through distinct pathological pathways: muscle mass loss appears associated with Aβ retention, while weakness correlates with WMH burden. Both mechanisms may ultimately contribute to cognitive impairment.[6] In line with earlier findings, a significant correlation between lower muscle mass and Aβ deposition was observed in key cortical regions such as the bilateral parietal, precuneus, and cingulate cortices.[98,99] In summary, cognitive impairment in older adults arises from complex neuropathological processes. In the context of sarcopenia, cerebral Aβ retention and gray and white matter alterations appear to function as key dynamic contributors to cognitive decline.[6]

Beyond Aβ and tau pathology, 18F-fluorodeoxyglucose (FDG)-PET has been employed to measure regional cerebral glucose metabolism, providing insights into metabolic dysfunction in neurodegenerative conditions.[49] Cerebral hypometabolism has been consistently documented in MCI, with the most pronounced reductions localized to posterior parietal and temporal regions.[100] Research has demonstrated that baseline hypometabolism in the right precuneus is associated with the rate of longitudinal memory decline.[101] Thus, FDG-PET may serve as a prognostic marker for tracking cognitive changes. In summary, PET imaging offers complementary biomarkers for sarcopenia-related cognitive impairment: Aβ and tau PET for molecular pathology, and FDG-PET for metabolic dysfunction. However, the existing evidence is primarily associative and cross-sectional. Future longitudinal studies integrating PET with other imaging modalities are needed to establish whether these molecular and metabolic changes precede or follow cognitive decline in sarcopenic patients.

Limitation and Prospect

Although significant progress has been made in researching the mechanisms and clinical comorbidity of sarcopenia and cognitive impairment, there is still much untapped potential in the deeper study of cognitive impairment in the context of sarcopenia, especially in terms of imaging. A key diagnostic challenge is that amyloid and tau pathology, present in sarcopenia-related cognitive impairment, are also hallmarks of other dementias including DLB and AD, making it difficult to isolate the contribution of sarcopenia alone from these concurrent pathologies.[102]

Second, several fundamental questions remain unresolved. It is uncertain whether imaging markers such as cerebral blood flow (CBF) actively contribute to the development of cognitive impairment in sarcopenia, exacerbate pre-existing symptoms, or simply predict the trajectory of cognitive decline. Furthermore, the relationship between sarcopenia severity, amyloid burden, and cognitive prognosis has yet to be clarified. These knowledge gaps are compounded by methodological limitations, including heterogeneous study designs and modest sample sizes, which constrain the interpretability and generalizability of existing findings. More specifically, although previous studies have suggested associations between brain structural or molecular alterations and muscle measures in sarcopenia, the findings have been inconsistent and provide only partial insight into the precise pathological mechanisms linking sarcopenia to cognitive impairment.[6]

Given the lack of imaging manifestations that facilitate the study of specific cognitive impairments in the context of sarcopenia using different imaging techniques, there is an urgent need for coordinated global research efforts to fill the existing knowledge gaps in this field. Examples include researching the imaging manifestations of cognitive impairment in the context of sarcopenia and the imaging-level correlation between sarcopenia and cognitive impairment. Emerging evidence indicates that specific components of sarcopenia, namely muscle mass, muscle power, and gait speed, exhibit distinct patterns of association with neuroimaging and pathological markers. Each sub-domain demonstrates unique relationships with Aβ burden, white matter hyperintensities (WMH), and brain atrophy in the context of cognitive impairment[6] which may serve as an important direction for future research. Additionally, in this emerging field, a systematic search protocol has not been widely adopted, and most available studies are derived from Asian populations, leaving generalizability to Western cohorts unclear. Direct evidence from neuroimaging studies in sarcopenic patients with cognitive impairment remains limited; the majority of evidence is extrapolated from studies on MCI or AD in general populations. Furthermore, contradictory or negative findings remain underreported. Addressing these gaps through multi-center longitudinal studies, diverse geographic representation, and direct imaging evidence in sarcopenic populations represents an important direction for future research.

Conclusion

In conclusion, this review supports the implementation of in-depth imaging-based assessment of cognitive function in patients with sarcopenia for both clinical and research purposes. Structural MRI studies have reported white matter hyperintensities and gray matter changes; diffusion MRI has revealed hippocampal connectivity disruption and white matter microstructural abnormalities; and PET has detected Aβ deposition and glucose hypometabolism. It may enable earlier risk identification, guide targeted interventions, and ultimately improve outcomes for the aging population affected by both conditions. However, current evidence remains largely associative, with few direct studies in sarcopenic populations and limited generalizability beyond Asian cohorts. From a clinical perspective, these imaging findings are not yet ready for routine use but may hold promise for future risk identification and intervention monitoring.

Generative AI Statement

The authors declare that no Generative AI was used in the creation of this review.

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Disclosure

Wen-Xuan Lei and Jing-Jun Zhu are co-first authors for this work. The authors declare that the review was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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