

Irisin and BDNF in Muscle and Cognitive Alterations in Cardiovascular Disease: Mechanistic Insights and Clinical Implications

Raissa Santana Dias Simões

Ariadne Augusta Maiente¹ Durvanei Augusto Maria² Raissa Santana Dias Simões¹ Adriano Cressoni Araújo¹ Elen L. Guiguer¹ Sandra M. Barbalho^{1, 3} ¹Universidade de Marília (UNIMAR); Marília; SP
²Instituto Butantan; São Paulo; SP ³Hospital Beneficente da UNIMAR; Marília; SP

RESUMO

Abstract Introduction: Cardiovascular diseases (CVD) are frequently associated with systemic alterations that extend beyond the heart, including skeletal muscle dysfunction and cognitive decline. Emerging evidence suggests that disrupted muscle-brain communication plays a key role in these complications. In this context, irisin, a myokine released during muscle contraction, and brain-derived neurotrophic factor (BDNF), a central regulator of neuroplasticity, have gained attention as important mediators linking metabolism, muscle, and cognitive health. **Objective:** This review aims to investigate the roles of irisin and BDNF in the interplay between muscle alterations and cognitive impairment in patients with cardiovascular disease, focusing on underlying mechanisms and clinical implications.

Methods: This narrative review was based on literature searches conducted in PubMed, EMBASE, and Web of Science using descriptors related to “irisin,” “BDNF,” “cardiovascular disease,” “sarcopenia,” and “cognitive decline.” Experimental, clinical, and review studies were selected based on relevance to molecular mechanisms and functional outcomes. Data were qualitatively synthesized. **Discussion:** In CVD, chronic inflammation, oxidative stress, and reduced physical activity can contribute to decreased irisin levels, impairing muscle metabolism and promoting sarcopenia. Reduced irisin may also limit the activation of signaling pathways involved in neuroprotection and synaptic plasticity. Concurrently, lower circulating and central levels of BDNF are associated with impaired neurogenesis, reduced synaptic function, and cognitive decline. Importantly, irisin has been shown to stimulate BDNF expression, suggesting a mechanistic link between skeletal muscle activity and brain function. This muscle-brain axis is further influenced by endothelial dysfunction and reduced cerebral perfusion, common in CVD, exacerbating both muscular and cognitive impairments. Clinical and experimental evidence indicate that interventions such as physical exercise can increase irisin and BDNF levels, thereby improving muscle function and cognitive performance. **Conclusion:** Irisin and BDNF play a central role in the interaction between muscle dysfunction and cognitive decline in cardiovascular disease. Targeting the muscle-brain axis through lifestyle and therapeutic strategies may represent a promising approach to mitigate both physical and cognitive impairments in this population

Palavras-chave: Irisin BDNF Cardiovascular Disease Sarcopenia Cognitive Decline.