BALTIC JOURNAL OF SPORT & HEALTH SCIENCES
No. 4(137); 2025; 55–56; ISSN 2351-6496 / eISSN 2538-8347
DOI: *https://doi.org/10.33607/bjshs.v4i137.1699*

Doctoral thesis abstract

Resistance Training and Muscle-Brain Crosstalk: Implications for Cognitive Decline in Aging and Spinal Cord Injury

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BACKGROUND AND OBJECTIVES

Exerkines are signalling factors that are released from organs throughout the body during physical exercise (El-Sayes et al., 2019). Some of these exerkines are thought to contribute to the well-documented benefits of exercise on brain health and cognitive function, potentially delaying age-related cognitive decline (Erickson et al., 2011). However, research is still far from establishing a mechanism-based, evidence-driven exercise programme to prevent such decline. To date, most studies have focused on endurance training, leaving other training modalities underexplored. Moreover, few studies have simultaneously examined exercise-induced effects on blood, brain, and cognitive domains, limiting more holistic understanding of the underlying mechanisms. Research has also primarily involved healthy adults, whereas older adults at risk of Mild Cognitive Impairment (MCI) are less frequently studied. Importantly, the effects of exercise on cognition have never been investigated in persons with Spinal Cord Injury (SCI), a population with an elevated risk of age-related cognitive decline and dementia.

The primary objective of the dissertation was therefore to gain a more comprehensive understanding of the mechanisms underlying the beneficial effects of exercise training, specifically resistance exercise in older adults and Neuromuscular Electrical Stimulation (NMES) in individuals with SCI, on brain health and cognitive function, with a particular focus on the role of exerkines in (exercise-induced) neuroplasticity.

METHODS

Eleven studies were conducted. *Study 1* was a literature review describing exerkine release following acute and chronic endurance or resistance exercise and their effects on neuroplasticity via long-term synaptic potentiation. *Study 2* summarised the findings from transcriptome and secretome studies identifying muscle-derived exerkines (myokines). *Studies 3* and *4* were cross-sectional studies in older adults (n = 74) investigating the relationships between participant characteristics, blood (inflammatory and neurotrophic) and brain biomarkers (neurometabolites, regional grey matter volumes), and cognitive function. *Studies 5–8* evaluated the effect of a single bout (n = 37) and a 12-week resistance exercise programme (n = 74) on blood and brain biomarkers and cognitive function in older adults. *Studies 6* and *7* further compared outcomes between cognitively healthy older adults and those at elevated risk of MCI (based on the Montreal Cognitive Assessment). *Study 9* systematically reviewed evidence on the effects of exercise interventions on cognitive performance in individuals with SCI and highlighted factors underlying their elevated risk of cognitive decline. *Study 10* tested the effect of a single bout of NMES on exerkines and cognitive performance in persons with SCI. *Study 11* described the protocol of a 12-week NMES intervention in individuals with SCI to examine the effect on exerkines and cognitive outcomes.

RESULTS

Study 1 identified 16 exerkines with known (in)direct effects on long-term synaptic potentiation. *Study 2* reported 1,126 putative myokines, most with still unknown effects on the brain and body. *Study 3* found associations between the circulating inflammatory marker kynurenine and signs of neuroinflammation and neurodegeneration in older adults. *Study 4* showed that older adults with normal-to-slightly-elevated body weight and greater handgrip strength maintained larger brain volumes. *Study 5* demonstrated improved working memory performance in older adults immediately after a single session of resistance exercise training compared to control group. *Study 6* suggested hippocampal volume preservation over time in the resistance exercise group, and *Study 7* revealed executive function improvements in older adults at elevated risk of MCI after 12 weeks of resistance training compared with control group. *Study 8* demonstrated neurometabolic changes in older adults who contracted COVID-19 during participation. *Study 9* confirmed that no prior studies have investigated exercise effects on cognitive function in individuals with SCI. *Study 10* found increases in lactate levels, but no changes in cognitive performance after a single NMES session in persons with SCI. *Study 11* described the design for a future 12-week NMES intervention study for individuals with SCI.

CONCLUSIONS

The dissertation advances the understanding of exercise effects on brain health and cognition in older adults and individuals with SCI, providing a neurobiological basis for future research. Kynurenine levels, handgrip strength, and a healthy body weight emerged as potential biomarkers of brain health for older adults. The findings underscore the importance of monitoring cognitive functioning in persons with SCI.

Although further research is needed to clarify the effect of different exercise modalities across populations with varying cognitive risk profiles, the present evidence reinforces the notion that physical exercise benefits brain function. A multimodal, enjoyable, and sustainable exercise programme maintained throughout life is likely to be the most effective strategy to mitigate or delay age-related cognitive decline.

Keywords: aging, cognition, myokines, exercise, spinal cord injury

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Received on September 10, 2025
Accepted on September 23, 2025