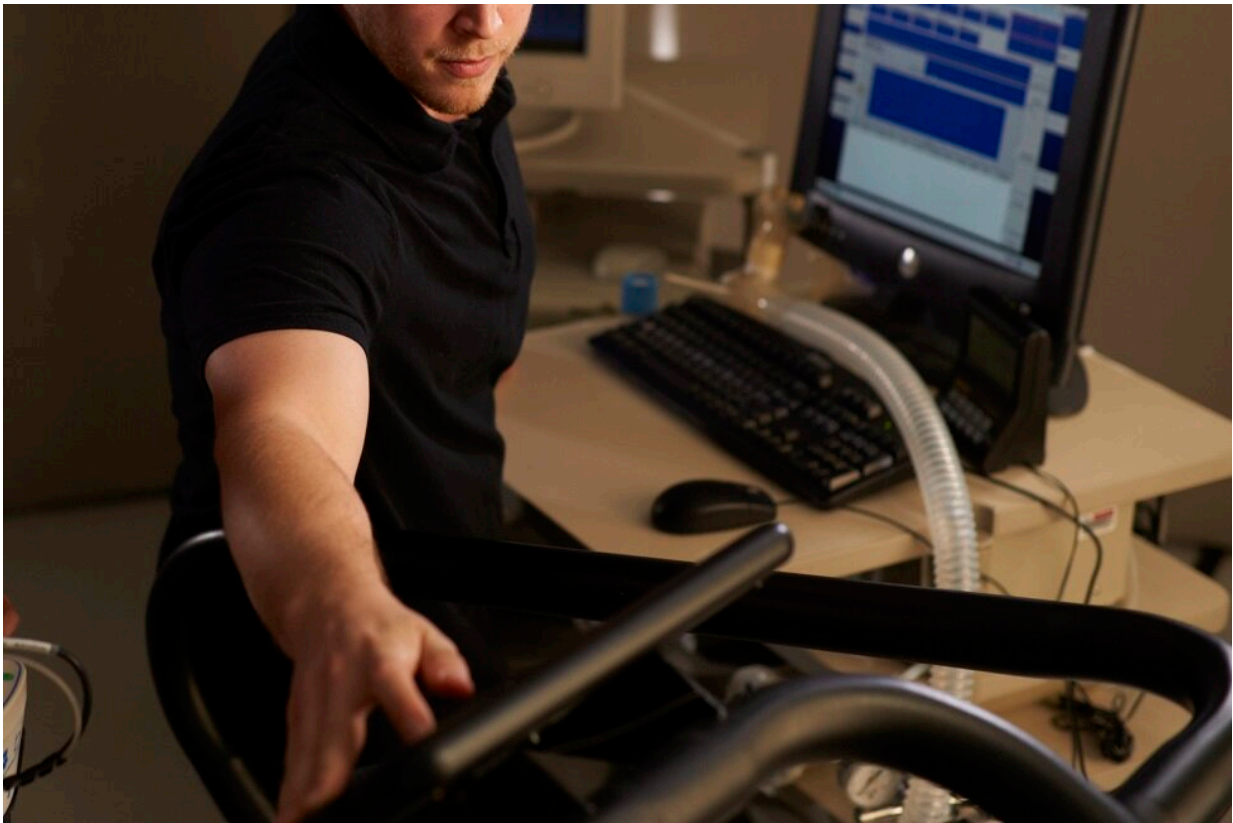


Memory biomarkers confirm aerobic exercise helps cognitive function in older adults

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The enhanced physical activity group underwent 26 weeks of supervised treadmill training. Blood samples for both groups were taken at baseline and after 26 weeks. Credit: Florida Atlantic University

Increasing evidence shows that physical activity and exercise training

may delay or prevent the onset of Alzheimer's disease (AD). In aging humans, aerobic exercise training increases gray and white matter volume, enhances blood flow, and improves memory function. The ability to measure the effects of exercise on systemic biomarkers associated with risk for AD and relating them to key metabolomic alterations may further prevention, monitoring, and treatment efforts. However, systemic biomarkers that can measure exercise effects on brain function and that link to relevant metabolic responses are lacking.

To address this issue, Henriette van Praag, Ph.D., from Florida Atlantic University's Schmidt College of Medicine and Brain Institute and Ozioma Okonkwo, Ph.D., Wisconsin Alzheimer's Disease Research Center and Department of Medicine at the University of Wisconsin-Madison and their collaborators, tested the hypotheses that three specific biomarkers, which are implicated in learning and memory, would increase in [older adults](#) following [exercise training](#) and correlate with cognition and metabolomics markers of [brain](#) health. They examined myokine Cathepsin B (CTSB), brain derived neurotrophic factor (BDNF), and klotho, as well as metabolomics, which have become increasingly utilized to understand biochemical pathways that may be affected by AD.

Researchers performed a metabolomics analysis in blood samples of 23 asymptomatic late middle-aged adults, with familial and genetic risk for AD (mean age 65 years old, 50 percent female) who participated in the "aeRobic Exercise And Cognitive Health (REACH) Pilot Study" (NCT02384993) at the University of Wisconsin. The participants were divided into two groups: usual [physical activity](#) (UPA) and enhanced physical activity (EPA). The EPA group underwent 26 weeks of supervised treadmill training. Blood samples for both groups were taken at baseline and after 26 weeks.

Results of the study, published in the journal *Frontiers in Endocrinology*,

showed that plasma CTSB levels were increased following this 26-week structured aerobic [exercise](#) training in older adults at risk for AD. Verbal learning and memory correlated positively with change in CTSB but was not related to BDNF or klotho. The present correlation between CTSB and verbal learning and memory suggests that CTSB may be useful as a marker for cognitive changes relevant to hippocampal function after exercise in a population at risk for dementia.

Plasma BDNF levels decreased in conjunction with metabolomic changes, including reductions in ceramides, sphingo- and phospholipids, as well as changes in gut microbiome metabolites and redox homeostasis. Indeed, multiple lipid metabolites relevant to AD were modified by exercise in a manner that may be neuroprotective. Serum klotho was unchanged but was associated with cardiorespiratory fitness.

"Our findings position CTSB, BDNF, and klotho as exercise biomarkers for evaluating the effect of lifestyle interventions on [brain function](#)," said van Praag, corresponding author, an associate professor of biomedical science, FAU's Schmidt College of Medicine, and a member of the FAU Brain Institute and the FAU Institute for Human Health & Disease Intervention (I-HEALTH). "Human studies often utilize expensive and low throughput brain imaging analyses that are not practical for large population-wide studies. Systemic biomarkers that can measure the effect of exercise interventions on Alzheimer's-related outcomes quickly and at low-cost could be used to inform disease progression and to develop novel therapeutic targets."

CTSB, a lysosomal enzyme, is secreted from muscle into circulation after exercise and is associated with memory function and adult hippocampal neurogenesis. Older adults with cognitive impairment have lower serum and brain CTSB levels. BDNF is a protein that is upregulated in the rodent hippocampus and cortex by running and is important for adult neurogenesis, synaptic plasticity, and [memory](#)

[function](#). Klotho is a circulating protein that can enhance cognition and synaptic function and is associated with resilience to neurodegenerative disease, possibly by supporting brain structures responsible for memory and learning.

"The [positive association](#) between CTSB and cognition, and the substantial modulation of lipid metabolites implicated in dementia, support the beneficial effects of exercise training on brain function and brain health in asymptomatic individuals at risk for Alzheimer's disease," said van Praag.

More information: Julian M. Gaitán et al, Effects of Aerobic Exercise Training on Systemic Biomarkers and Cognition in Late Middle-Aged Adults at Risk for Alzheimer's Disease, *Frontiers in Endocrinology* (2021). [DOI: 10.3389/fendo.2021.660181](https://doi.org/10.3389/fendo.2021.660181)

Provided by Florida Atlantic University

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