Aerobic Fitness and Healthy Brain Aging
Cognition, Brain Structure, and Dopamine

Lars Jonasson

Akademisk avhandling

som med vederbörligt tillstånd av Rektor vid Umeå universitet för avläggande av medicine doktorsexamen framläggs till offentligt försvar i Sal 933, NUS byggnad 3B, fredagen den 29 September, kl. 13:00.
Avhandlingen kommer att försvaras på engelska.

Fakultetsopponent: Professor, Emrah Düzel,
Institute of Cognitive Neurology and Dementia Research, University Hospital Magdeburg, Magdeburg, DE.

Department of Radiation Sciences
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**Abstract**

**Background** Performing aerobic exercise and maintaining high levels of aerobic fitness may have positive effects on both brain structure and function in older adults. Despite decades of research however, there is still a rather poor understanding of the neurocognitive mechanisms explaining the positive effects of aerobic exercise on cognition. Changes in prefrontal gray matter as well as dopaminergic neurotransmission in striatum are both candidate neurocognitive mechanisms. The main aims of this thesis are: 1. To investigate the effects of aerobic exercise and fitness on cognition and magnetic resonance imaging (MRI) derived gray matter volumes using data from a 6 month physical exercise intervention in older adults (Study I). 2. To simulate the effect of atrophy in longitudinal positron emission tomography (PET) which could pose a challenge to interpreting changes in longitudinal PET imaging (Study II). 3. To study the influence of aerobic exercise and fitness on the dopamine D2-receptor (D2R) system in striatum using \[11C\]raclopride PET as a potential mechanism for improved cognition (Study III).

**Results** In Study I, aerobic exercise was found to improve cognitive performance in a broad, rather than domain-specific sense. Moreover, aerobic fitness was related to prefrontal cortical thickness, and improved aerobic fitness over 6 months was related to increased hippocampal volume. In Study II, we identified areas in the striatum vulnerable to the effect of shrinkage, which should be considered in longitudinal PET imaging. Finally, in Study III, the effect of being aerobically fit, and improving fitness levels was found to impact dopaminergic neurotransmission in the striatum, which in turn mediated fitness-induced improvements in working memory updating performance.

**Conclusion** The findings in this thesis provide novel evidence regarding the neurocognitive mechanisms of aerobic exercise-induced improvements in cognition, and impacts the interpretation of longitudinal PET imaging. Performing aerobic exercise and staying aerobically fit at an older age have positive effects on cognition and brain systems important for memory and cognition. Specifically, fitness-induced changes to the dopaminergic system stands out as one novel neurocognitive mechanism explaining the positive effects of aerobic fitness on working-memory performance in healthy older adults.

**Keywords**

Aerobic exercise, VO2, working memory, executive function, freesurfer, striatum, dopamine, D2-receptors, \[11C\]raclopride