

Reasoning of dissertation topic and competency of potential supervisor for admission onto joint LSU and TU doctoral studies in 2020

Area of research (title and code)	Biomedical sciences B000
Field of research (title and code)	Biology 01B
Topic of research	Healthy Ageing (health promotion)
Institution	Lithuanian sports university

Potential supervisor

Pedagogical and scientific degree	Name, surname	Academic position
Prof. Dr.	Oron Levin	Prof.

Short reasoning of proposed dissertation topic

Title
Resistance training as a means to improve muscle and brain health in individuals with mild cognitive impairments
<p>Short research description (including aims and objectives) (maximum 1500 characters).</p> <p>Ageing is accompanied by cognitive declines that can further develop into dementia. These declines could be alleviated by physical exercise intervention. The fact that exercise is “sensed” by the brain suggests that muscle-induced peripheral factors, which are produced during and/or after the exercise has the potential to restore brains’ structural and functional integrity, potentially through activation of endocrine loops; e.g., the “muscle-brain crosstalk” model (see: BK Pedersen. Nat Rev Endocrinol. 15, 383-392, 2019). For example, increased expressions of serum brain-derived neurotrophic factor (BDNF) and insulin-like growth factor-1 (IGF-1) were found to be associated with exercise-induced changes in hippocampal neurogenesis, which may partly explain the positive impact of exercise on cognition. This project aims to explore the underlying mechanisms by examining potent associations between exercise-related muscle biomarkers, endocrine factors, and brain integrity biomarkers.</p> <p>The objectives of the current research project are:</p> <ul style="list-style-type: none"> • Establish neurobiological model of cognitive and motor impairments in older adults with mild cognitive impairments (MCI) (<i>Stage 1</i>, observation). • Examine the mechanisms the beneficial effect of strength training on cognition and motor function in older adults with MCI and suggest muscle-brain endocrine loop that may be relevant for mediating these beneficial effects (<i>Stage 2</i>, intervention). • Based on findings from <i>Stage 1</i> and <i>Stage 2</i>, establish a model of muscle-brain crosstalk for improving brain and neuromuscular integrity of individuals with risk of dementia.
<p>Relevance of the problem, its novelty at national and international level (maximum 1500 characters).</p> <p>Mild cognitive impairment (MCI) is a condition where cognitive abilities may deteriorate beyond what is normally expected in normal ageing. Physical activity appears, nonetheless, to reduce the prevalence of cognitive declines and dementia. Since current research into physical activity in ageing lack a holistic design approach, there is an urgent need to identify and classify brain, endocrine, and muscle biomarkers that reflect physiological response to physical activity at different organ systems. Exploring the effects of exercise on metabolic and endocrine processes that have a major influence on muscle and brain integrity is a necessary step towards development of intervention protocols for improving cognitive abilities and reducing the risk for dementia in older age. We will focus on the effects of intervention with strength training on brain, blood and muscle metabolites in older adults with MCI. Specifically, associations between biomarkers for integrity of brain and neuromuscular systems will be examined using: (1) proton magnetic resonance spectroscopy to study the effect of intervention on brain metabolites and neurotransmitters (such as myo-inositol) as indicators for brain integrity. (2) Serum levels of c-terminal peptide agrin fragment (CAF) as an indicator for integrity of the neuromuscular junction. (3) Serum levels of BDNF, IL-6 and PGC1α-kynurenine as possible</p>

mediators of neuroplasticity and neurogenesis in brain and muscles. We will focus specifically on the underlying mechanisms of strength training gains since accumulating evidence have pointed to this type of intervention as a potent and robust preventive strategy against both sarcopenia and cognitive impairments in older age.

Research methods and possibilities for conducting these studies (maximum 1500 characters).

- Questionnaire to assess: a) health (WHO 100); b) physical activity (IPAQ); c) Depression and Anxiety (HADS); d) mood (POMS). Montreal Cognitive Assessment (MoCA) for MCI.
- Determination of body composition (Tanita TBF-300).
- Magnetic resonance imaging (MRI). Data will be collected using a 3 Tesla scanner Siemens) with a 16 channel head coil. MRI will include:
 - a) Anatomical scans T1 and T2 weighted images to study regional changes in brain volume.
 - b) Proton - MR spectroscopy (1H-MRS) for detection of endogenous metabolites in the human brain.
- We will focus on neurometabolites that could serve as indicators of neuronal abnormalities in MCI; specifically: myo-inositol (mI), N-acetylaspartate (NAA) and choline (Cho).
- Blood sampling (ELISA, Biotek, model ELX 800): brain-derived neurotrophic factor (BDNF), Creatine kinase (CK), C-reactive protein (CRP), C-terminal fragment of agrin (CAF), Cortisol (C), Interleukin-6 (IL-6), Insulin-like growth factor 1 (IGF-1), Kynurenine (KYN), Testosterone (T), Tumor necrosis factor alpha (TNF-a).
- Cognitive tests (ANAM4): memory evaluation, mathematical processing (attention/executive function), and reaction time.
- Fitness Fullerton Test battery for the seniors.

Please indicate the links between the proposed topic for the doctoral thesis and health promotion / physical therapy / sports study programs.

The topic related lectures will be covered in the following modules for master students:

“Skeletal muscle and motor control” (Sports Physiology and Genetics, Sports Coaching, and Physiotherapy study programmes), module coordinator assoc. prof. N. Masiulis;

“Methodology for the development of motor and cognitive functions” (Physical Activity and Public Health and Physiotherapy study programs), module coordinator assoc. prof. V. Česnaitienė;

Is the proposed topic for the doctoral thesis related to currently funded research projects?

The proposed topic is based on the currently funded project of the 3rd call of the national research programme 'HEALTHY AGEING'. Topic: “*Resistance training as a means to improve muscle and brain health in individuals with mild cognitive impairments*”. Proposal registration No. P-SEN-20-29.

Is the proposed topic for the doctoral thesis related to joint research with a foreign institution?

The following researchers will be directly involved in this project:

Prof. Mati Paasuke, Professor of Kinesiology and Biomechanics at the University of Tartu, Tartu, Estonia.

Prof. Uwe Himmelreich, Professor in the Department of Imaging and Pathology and head of the Biomedical MRI Unit at the Faculty of Medicine, KU Leuven, Leuven, Belgium.

Prof. Werner F. Helsen, Department of Movement Sciences, Movement Control & Neuroplasticity Research Group, KU Leuven, Leuven, Belgium.

Prof. Filip Staes, Department of Rehabilitation Sciences, Musculoskeletal Rehabilitation Research Group, KU Leuven, Leuven, Belgium.

Currently I am supervisor of 0 doctoral students.

Supervisor



(Signature)

Prof. Oron Levin

(Name, surname)

Date 2020-03-31