Reasoning of dissertation topic and competency of potential supervisor for admission onto joint LSU and TU doctoral studies in 2021

Area of research (title and code)	Biomedical sciences B000
Field of research (title and code)	Biology 01B
Topic of research	Health promotion, physiotherapy
Institution	Lithuanian sports university

Potential supervisor

Pedagogical and scientific degree	**Name, surname**	**Academic position**
Prof. Dr.	Nerijus Masiulis	Prof.
Co-supervisor Dr.	Oron Levin	Prof.

Short reasoning of proposed dissertation topic

Title
High and low intensity resistance training as a means to improve brain and muscle functions
Short research description (including aims and objectives) (maximum 1500 characters). The project will focus on the underlying mechanisms that mediate brain neurogenesis following high intensity (accentuated eccentric load, AEL) and low intensity (blood flow restriction training, BFRT) in healthy individuals. There is growing evidence that resistance training (RT) induces substantial brain changes which contribute to improved cognitive functions (Herold et al., 2019). BFRT when compared to regular RT is expected to result in lower risk of muscle damage (Loenneke et al., 2014), while having the beneficial same effect on muscle strength and possibly cognitive function (Törpel et al., 2018). Therefore, it is hypothesized that beneficial effect of BFRT on both muscle and brain integrity will be higher than that achieved with RT alone as the former is expected to induce less inflammatory effects and maximize effect of intervention on muscle-brain crosstalk. We will focus specifically on the effects of resistance training on brain neuroplasticity and function as well as neuromuscular adaptation since current body of knowledge on the effect of this intervention on muscle-brain crosstalk is limited.
Relevance of the problem, its novelty at national and international level (maximum 1500 characters). Increasingly, studies have been searching for the mechanism underlying the beneficial effect of exercise on brain health and cognition. Recent studies have advocated that myokines and exerkines probably mediate at least part of this effect (Pedersen, 2019; El-Sayes et al., 2019; Vints et al., 2022). By now, over 600 myokines have been discovered. Currently, only some of them were proven to cross the blood brain barrier or exert indirect effects on the brain. The most extensively studied examples are BDNF and IGF-1. Both were consistently reported to improve cognition and induce synaptic plasticity, neurogenesis and neural survival. These neurotrophic factors can be released from muscle tissue, but are also released from the brain itself. Given the abovementioned, there is an urgent need to identify and classify a wide range of biomarkers that reflect physiologic responses to physical activity and can be used in population-based studies in order to select the recommended forms of exercise to prescribe. This, nonetheless, requires prior knowledge of the effects of exercise on metabolic processes that have a major influence on muscle and brain performance (in general) and muscle-brain crosstalk (in particular) in order to develop "tailored" exercise programs that will fit the specific needs of the various and diverse ageing populations. Specifically, associations between biomarkers for integrity of brain and neuromuscular systems will be examined using (partial list): (1) 1H-MRS brain metabolites and neurotransmitters as indicators for brain structural/functional 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 mediators of muscle-brain crosstalk. Data will be

further analyzed to examine brain-muscle crosstalk in relation to the beneficial effect of training on cognitive function, motor functions, integrity of neuromuscular system, health-related physical fitness, and changes in biomarkers and hormonal levels. 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 sarcopenia and mobility declines.

References:

El-Sayes, J., Harasym, D., Turco, C. V., Locke, M. B., & Nelson, A. J. (2019). Exercise-induced neuroplasticity: a mechanistic model and prospects for promoting plasticity. *The Neuroscientist*, 25(1), 65-85.

Pedersen BK (2019). Physical activity and muscle–brain crosstalk. *Nature Reviews Endocrinology*, 15, 383–392.

Herold, F., Törpel, A., Schega, L., & Müller, N. G. (2019). Functional and/or structural brain changes in response to resistance exercises and resistance training lead to cognitive improvements–a systematic review. *European Review of Aging and Physical Activity*, 16(1), 1-33.

Törpel A, Herold F, Hamacher D, Müller NG, Schega L. (2018). Strengthening the Brain—Is Resistance Training with Blood Flow Restriction an Effective Strategy for Cognitive Improvement? *Journal of Clinical Medicine*, 7(10):337.

Loenneke, J. P., Thiebaud, R. S., & Abe, T. (2014). Does blood flow restriction result in skeletal muscle damage? A critical review of available evidence. *Scandinavian Journal of Medicine & Science in Sports*, 24(6), e415-422.

Vints, W. A. J., Levin, O., Fujiyama, H., Verbunt, J., & Masiulis, N. (2022). Exerkines and long-term synaptic potentiation: Mechanisms of exercise-induced neuroplasticity. *Frontiers in Neuroendocrinology*, 66, 100993.

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

1. Questionnaire to assess: (a) health (WHO 100); b) physical activity (IPAQ); c) Depression and Anxiety (HADS); (d) mood (POMS).
2. Determination of body composition (Tanita TBF-300).
3. Magnetic resonance imaging (anatomical MRI): proton-magnetic resonance spectroscopy (1H-MRS) and anatomical MRI. Data will be collected using a 3 Tesla (3T) MR scanner (Model: Siemens 3T Skyra) with a 16 channel head coil.
4. Blood sampling (ELISA, Biotek, model ELX 800): brain-derived neurotrophic factor (BDNF), Creatine kinase (CK), C-terminal fragment of agrin (CAF), Cortisol (C), Interliaukin-6 (IL-6), Insulin-like growth factor 1 (IGF-1), Kynurenine (KYN), Testosterone (T), Tumor necrosis factor alpha (TNF-a).
5. Cognitive tests (ANAM4): memory evaluation, mathematical processing (attention/executive function), and reaction time. Evaluation of motor-cognitive function interaction using dual task method.
6. Ultrasound imaging of thigh muscles will be used for quantification of muscle geometrical properties such as fascicle length, fascicle angle, tendon thickness (Esaote MyLab 50 XVision, Italy).
7. Tensiomyography (TMG) will be used for neuromuscular adaptation of muscle training.
8. BFRT, AEL training interventions.

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 <u>for master students</u>:

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

"Skeletal muscle and genetics" (Sports Physiology and Genetics, Sports Coaching and Physiotherapy study programmes), module coordinator prof. A. Ratkevičius;

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

<u>For bachelor students:</u>

"Cardiofitness and strength training" (European Bachelor of Physical Activity and Lifestyle study programme), module coordinator assoc. prof. N. Masiulis;

"Health enhancing physical activity" (Physical Activity and Public Health study programme), 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 two currently funded projects:

(1) **"Strength training and skeletal muscle-brain interaction".** Proposal registration No. P-MIP-21-355; (Research Council of Lithuania). 149005 EUR.

(2) **„Adaptation of the international tests batteries for the assessment of physical capacity of adults (18-64 years) and the elderly (65 years and older) and preparation of recommendations for use in Lithuania".** Proposal registration No. S-564; (Health Promotion Fund under the Ministry of Health of The Republic of Lithuania). 36000 EUR.
Is the proposed topic for the doctoral thesis related to joint research with a foreign institution? This study will be performed together: **Prof. Oron Levin**, Department of Rehabilitation Sciences, Musculoskeletal Rehabilitation Research Group, KU Leuven. **Prof. Mati Paasuke**, Professor of Kinesiology and Biomechanics at the University of Tartu, Tartu, Estonia. **Prof. Jeanine Verbunt,** Department of Rehabilitation Medicine Research School CAPHRI, Maastricht University, The Netherlands**.** **Prof. Gal Ziv**, The Academic College at Wingate, Netanya, Israel.

I am currently supervisor of 2 doctoral students.

Supervisor  Prof. Nerijus Masiulis

(signature) (Name, surname)

Date 2022-05-06