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
Assoc. Prof. Dr.	Nerijus Masiulis	Assoc. Prof.

Short reasoning of proposed dissertation topic

Title
Resistance training and muscle - brain crosstalk
Short research description (including aims and objectives) (maximum 1500 characters). There is growing evidence that regular resistance training (RT) contributes to improved cognitive functions. The understanding of how brain neurogenesis, cognition, and motor abilities are affected by RT is, nevertheless, limited. For example, it is not clear whether regular exercise training slows the trajectory of normal ageing by influencing metabolic and vascular risk factors, or whether it repetitively boosts brain function by inducing neurochemical and structural changes, or both. The fact that exercise responds by the brain suggests that muscle-induced peripheral factors enable, at least in part, direct crosstalk between muscles and brain. The current project is driven by the idea that understanding the mechanisms through which muscle and brain interact could offer new approaches to magnifying the beneficial and detrimental effects of RT on health at older age. Specifically, we aim at identifying brain, blood, and muscle biomarkers that could serve as predictors of response to exercise training at both muscular and brain levels and study the associations between those biomarkers in order to suggest a physiological models of exercise-induced muscle-brain crosstalk in ageing. These physiological model will be used further to examine whether the application of a relatively new method - blood flow restriction training (BFRT) will result in lower risk of muscle damage, while having the beneficial same effect on muscle strength and cognitive function as high intensity RT. 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.
Relevance of the problem, its novelty at national and international level (maximum 1500 characters). The official health bodies (e.g., World Health Organization – WHO) have published guidelines for exercise for people aged 65 and over. These guidelines comprise ≥150 minutes a week of moderate-intensity aerobic exercise, ≥three times a week of balance exercise, and ≥twice a week of resistance training (RT). The latter is of particular importance since besides reducing the negative impact of sarcopenia on daily life activities, RT it is also beneficial for improving balance control and cognition. On the down side, high-intensity RT may cause muscle damage. However, this negative effects may be elevated by low-intensity BFRT. Given the abovementioned, there is an urgent need to identify and classify a wide range of biomarkers that reflect physiologic responses to RT in general and BFRT in particular that can be in order to select the recommended forms of exercise regimes. 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.

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. Anatomical magnetic resonance imaging (anatomical MRI) and proton-magnetic resonance spectroscopy (1H-MRS). Data will be collected using a 1.5 Tesla (1.5T) MR scanner (Model: Philips Multiva) with a 16 channel head coil.
4. 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), Interliaukin-6 (IL-6), Insulin-like growth factor 1 (IGF-1), Kynurenine (KYN), Testosteron (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, and muscle thickness (Esaote MyLab 50 XVision, Italy).
7. Static posturography (Kistler, 9286).
8. Electrically evoked contractile properties of thigh muscles (MG 440, Medicor).
9. Evaluation of motor functions: determination of maximal strength (5 repetitions maximum (RM)); Isometric, Concentric (at 60^{O}/s), Eccentric (at 60^{O}/s) peak torque, Rate of force development (RFD), (Biodex Pro 3); Hand-grip test (Lafayette, 78010);
10. Fitness Fullerton Test battery for the senior: to evaluate impact of strength training on ability to perform motor control in everyday life.
11. RT, BFRT and power 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 for master students:
"Skeletal muscle and motor control" (Sports Physiology and Genetics, Sports Coaching and Physiotherapy study programmes), module coordinator assoc. prof. N. Masiulis;
"Skeletal muscle and genetics" (Sports Physiology and Genetics, Sports Coaching and Physiotherapy study programmes), module coordinator assoc. 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;
For bachelor students:
"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 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?

This study will be performed together with **Prof. Mati Paasuke**, Professor of Kinesiology and Biomechanics at the University of Tartu, Tartu, Estonia.

Intensive cooperation will continue with **Prof. Werner F. Helsen**, Department of Movement Sciences, Movement Control & Neuroplasticity Research Group, KU Leuven, Leuven, Belgium and **Prof. Filip Staes**, Department of Rehabilitation Sciences, Musculoskeletal Rehabilitation Research Group, KU Leuven, Leuven, Belgium.

Currently I am supervisor of 2 doctoral students.

Supervisor  Assoc. Prof. Nerijus Masiulis

(signature) (Name, surname)

Date 2020-03-31