

INCREASED EXERCISE INTENSITY DURING INTERVAL ROBOT-ASSISTED GAIT THERAPY IN SPINAL CORD INJURED PERSONS

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Background: Exercise intensity (in terms of cardiometabolic load) is relatively low during current 30-min continuous Robot Assisted Gait Therapy (RAGT)(1). This may in part limit the effectiveness of RAGT induced gait improvement in individuals with incomplete spinal cord injury (iSCI). Exercise intensity may be increased by applying interval exercise with high intensity exercise bouts. Objective: To determine if high intensity interval RAGT is feasible and to evaluate if muscle activity and cardiometabolic load are higher than during continuous exercise. Subjects: Nine subjects with iSCI (ASIA impairment scale C or D). Methods: All subjects performed a 30-minute interval exercise and a 30-minute continuous exercise in the Lokomat. During both sessions EMG activity of the lower-limb muscles and different cardiorespiratory responses (%HRR, VO₂, VCO₂, VE and RER) were obtained. Furthermore, all patients filled out the Borg-scale for rate of perceived exertion (RPE) and a self-developed questionnaire about their experiences with both sessions. Results: All subjects successfully completed the interval exercise on the Lokomat. Both the muscle activity and the cardiorespiratory responses were increased during the interval exercise compared to the continuous exercise, although for the muscle activity this difference was not significant. During the interval exercise, subjects' average %HRR was more than 15% higher than during the continuous exercise (33.6% vs. 18.0%). Besides, during the interval exercise subjects exercised almost half of the time (48%) above levels of aerobic exercise (>30% HRR), while this percentage was only 8% during the continuous exercise. In addition, the RPE was significantly higher after the interval session (mean 12.8 (1.3)) than during the interval session (mean 10.9 (1.7)). Nevertheless, 78% of the subjects preferred the interval session over the continuous session. Conclusion: Persons with iSCI can perform a high intensity interval RAGT. Besides, this study clearly demonstrates that the cardiometabolic load during this interval exercise is higher than during a continuous exercise. In addition, the cardiometabolic load during the interval exercise was high enough to reach levels of aerobic exercise, which may lead to an increased exercise capacity. Future research should clarify whether this type of RAGT exercise is effective in regaining walking ability for persons with iSCI. 1. F. Hoekstra et al. Effect of robotic gait training on cardiorespiratory system in incomplete spinal cord injury, *J. Rehabil Res Dev*, 50(10) pp. 1411-1422, 2013.

THE IMPACT OF SIMVASTATIN ON INSULIN SENSITIVITY IN PATIENTS WITH AND WITHOUT MYALGIA

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Introduction Simvastatin is a commonly prescribed cholesterol-lowering drug used to reduce the risk of cardiovascular disease. Despite the beneficial effects of simvastatin, adverse effects such as myalgia, muscle cramps, and fatigue have frequently been reported (1). Occurrence of the aforementioned adverse effects may inhibit a physically active lifestyle, which may further maintain or potentially worsen an already unhealthy way of living. The aim of this study is to investigate if insulin sensitivity is affected in subjects with or without simvastatin-associated myalgia. We hypothesize that subjects with myalgia, not without, have impaired insulin sensitivity, as shown in the study from Mallinson et al. (2), where subjects with myalgia had impaired insulin sensitivity compared to healthy non-statin users. Methods We will include 60 subjects with normal glucose tolerance undergoing treatment with simvastatin to participate in three separate trial days. The study is presently ongoing and 16 subjects have been completed. The subjects were divided into two groups based on the presence or absence of self-reported myalgia assessed by VAS-score. DXA-scan was used to measure body composition. Whole body stimulated glucose uptake was assessed by the hyperinsulinemic euglycemic clamp technique. A constant insulin infusion was administered intravenously over 2 hours with a concentration of 80 mU/m²/min and IV glucose was given at variable rates to keep the blood sugar at a constant level of 5.6 mM. Maximal whole body stimulated glucose uptake was calculated as the average glucose infusion rate during the last 30 min. Results 9 subjects with myalgia (5 M/4 F; age 61 +/- 2 years; weight 91 +/- 8 kg; BMI 30 +/- 2; fat % 38 +/- 4; FFM 56 +/- 4 kg; VAS 4.6 +/- 0.9) and 7 without myalgia (5 M/2 F; age 58 +/- 3 years; weight 86 +/- 8 kg; BMI 28 +/- 2; fat % 31 +/- 3; FFM 60 +/- 5 kg; VAS 0.1 +/- 0.1) have completed the study. GIR values were similar, 11 +/- 1 and 13 +/- 1 mg/min/kg FFM, in the group with and without myalgia, respectively. By using FFM instead of body weight, we corrected for the differing body compositions between the male and female subjects, but GIR values per body weight were also similar. Discussion At this point, our results do not demonstrate any statistically significant differences in insulin sensitivity between the group with simvastatin-associated myalgia and the group without. Apart from the VAS-scores, groups were comparable for all parameters measured. Additional subjects are needed in order to draw any final conclusions. References (1) Franc S et al. (2003) *Cardiovasc Drugs Ther.* 17(5-6), p 459-465 (2) Mallinson JE et al. (2015) *J Physiol.* Contact mimmi@sund.ku.dk

Oral presentations

OP-PM10 Physiology: Age II

EFFECT OF HIGH INTENSITY TRAINING AND ISOINERTIAL TRAINING ON INTERMUSCULAR ADIPOSE TISSUE IN OLDER ADULTS.

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Introduction Recent findings suggest that, in elderly, Intermuscular Adipose Tissue (IMAT) may be associated with inactivity and that exercise training may be able to mitigate the content of IMAT (Murphy et al., 2012; Santanasto et al., 2011). The purpose was to determine how IMAT can be influenced by exercise and if a greater reduction in IMAT occurs with concurrent aerobic High Intensity Training (HIT) and Isoinertial Resistance Training (IRT). Methods 12 moderately active older adults (age: 69.4±4.3 yy; weight: 78.5±10.5 kg; height: 171.2±5.3 cm; BMI: 22.9±2.7 kg/m²; V'O₂max: 29.5±4.1 mL/kg/min) were exposed to 8 weeks of: i) HIT training with 7 two-minute cycling repetitions at 90% of V'O₂max, 3 times/week and, after 4 months, ii) IRT performed with an isoinertial leg press (YoYo Technology AB) comprised 4x7 maximal concentric-eccentric knee extensions, 3 time/week. MRI of the mid-thigh was examined to determine changes in muscle composition (Cross Sectional Area (CSA) and IMAT) after exercise intervention using SliceOmatic image analysis software (Rossi et al., 2010). IMAT was defined as adipose tissue area visible between quadriceps muscle groups. Results Quadriceps CSA increased

significantly after HIT and after IRT by 6% ($P < 0.05$) and 7% ($P < 0.05$) respectively. IMAT decreased after HIT and IRT by 31% ($P < 0.05$) and 41% ($P < 0.05$) respectively. Net thigh lean mass increased significantly after both training by 10% ($P < 0.05$). Discussion Our data, in contrast with Jacobs (2014) and Goodpaster (2008) but in agreement with other previous studies (Murphy et al., 2012; Santanasto et al., 2011), show that IMAT decrease after a 8 weeks exercise intervention in older adults both after HIT and IRT. Preliminary data show that exercise training performed at high intensity in older adults may contrast skeletal muscle fat infiltration. Our study is non-randomized, not-counterbalanced and limited by small sample size: additional studies are needed to determine the most effective exercise (type, intensity, modalities) able to decrease IMAT and how this decrease may positively affect health in elderly. References Goodpaster B, Chomentowski P, Ward B, Rossi A, Glynn NW, Delmonico MJ, Kritchevsky SB, Pahor M, Newman AB. (2008). *J Appl Physiol*, 105(5), 1498-1503. Jacobs JL, Marcus RL, Morrell G, LaStayo P. (2014). *Biomed Res Int*, 398960. Murphy JC, McDaniel JL, Mora K, Villareal DT, Fontana L, Weiss EP. (2012). *J Appl Physiol*, 112(1), 79-85. Rossi A, Zoico E, Goodpaster BH, Sepe A, Di Francesco V, Fantin F, Pizzini F, Corzato F, Vitali A, Micciolo R, Harris TB, Cinti S, Zamboni M. (2010). *Obesity*, 18(12), 2379-84. Santanasto AJ, Glynn NW, Newman MA. (2011). *Journal of Obesity*, 516576.

BLOCKING ANGIOTENSIN II TO IMPROVE THE ACUTE MUSCLE RESPONSE TO EXERCISE IN ELDERLY MEN

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Title Blocking angiotensin II to improve the acute muscle response to exercise in elderly men Introduction The molecular mechanisms behind sarcopenia are largely unknown. Satellite cells (SC) are important for the plasticity and regenerative capacity of skeletal muscle and the decline in SC function with age is associated with increased Transforming Growth Factor-beta (TGF-beta) signalling [1]. Blocking Angiotensin II (AngII) in sarcopenic mice has been reported to downregulate TGF-beta and upregulate Insulin-like Growth Factor-1 (IGF-1) signalling in remodelling skeletal muscle [2], suggesting that blocking AngII could enhance muscle adaptation to loading. This has not previously been investigated in human skeletal muscles. The aim of this study was to investigate the effect of blocking AngII on the acute response of muscle to exercise in elderly men. Methods 26 elderly healthy men (+64 years) were recruited and assigned to an AngII blocker (Losartan) or Placebo group using stratified randomization according to age, BMI and ACE genotype. Losartan (100mg/day) or placebo was consumed for 18 days. Participants performed one bout of heavy one-legged resistance exercises, consisting of 5x12 repetitions of concentric work (70% of 1RM) and 4x6 repetitions of eccentric work (110% of 1RM). Six muscle biopsies were obtained from each subject from the Vastus Lateralis muscles: before (baseline) and after one week of treatment with Losartan, and after exercise at 4 hours and on days 1, 4 and 7. Blood pressure and blood samples were collected at the same six time points. Biopsies were sectioned and stained for Pax7, type I myosin and laminin for enumeration of SC associated with type I and type II fibres. mRNA levels of Tenascin-C, TGF-beta, IGF-1, and Collagen I were determined by real time PCR. Data were analysed by 1 or 2 way repeated measures ANOVA. Results There was no significant effect of Losartan on the SC response to exercise, but a main effect of time for SC per type I fibre was found, with increases on days 4 and 7 after exercise. No significant effect of Losartan was found for gene expression levels of Tenascin-C, TGF-beta, IGF-1, or Collagen I. Losartan treatment resulted in a small drop in diastolic blood pressure. Discussion Contrary to our hypothesis we did not find any effect of Losartan on the muscle response to acute exercise. However, it is possible that treatment and exercise over a longer period of time are required in order to be able to detect an effect. A study is currently underway to investigate this. References 1. Carlson, M.E., et al., *EMBO Mol Med*, 2009. 1(8-9): p. 381-91. 2. Burks, T.N., et al., *Sci Transl Med*, 2011. 3(82): p. 82ra37. Contact mette.flindt@regionh.dk

MATTERS OF FIBRE SIZE AND MYONUCLEAR DOMAIN; DOES SIZE MATTER MORE THAN AGE?

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Introduction The relationship between skeletal muscle fibre size and myonuclear content is poorly understood, and may be influenced by ageing and life-long endurance exercise. Data from muscle biopsy cross-sections are typically reported as biopsy means, overlooking the great variability in fibre size (Mackey et al., 2014) and potentially the size-specific changes with age (Brack et al., 2005). The aim of this study was to gain more insight in the relationship between fibre size and myonuclei in a group of master athletes, age-matched controls and younger counterparts. Methods 49 subjects were recruited into 4 groups as young/old and endurance trained/untrained. A biopsy was obtained from the vastus lateralis muscle of each individual, sectioned and stained by immunohistochemistry for determination of fibre area and the number of myonuclei per fibre (MN/F). Myonuclear domain (MND) was calculated from these data. The MN/F and MND data were divided into clusters according to different ranges in fibre size: 3 large 2000 μm^2 clusters, and 20 small 500 μm^2 clusters. Clusters were analyzed by a 1-way ANOVA. Results The 2000 μm^2 analysis revealed that in fibres of comparable size there were no differences in MN/F or MND between the 4 groups. Therefore the groups were pooled, revealing a greater MN/F and a larger MND in medium vs. small fibres, but also in large vs. medium fibres. The 500 μm^2 analysis indicated a strong linear relationship between MN/F and fibre area. MND was non-linearly related to fibre area, with a markedly smaller domain in fibres $< 3000 \mu\text{m}^2$. A larger proportion of type II fibres $< 3000 \mu\text{m}^2$ was observed in the old. Discussion In contrast to (Brack et al., 2005) we did not observe age-related differences in MN/F in fibres of similar size, and there was no effect of life-long endurance training on myonuclear content. The strong linear relationship between fibre size and MN/F indicate that changes in fibre size are followed by changes in myonuclear content (or the other way around). The MND findings suggest that age-related reductions in MND could be explained by a larger proportion of small fibres, and highlight the usefulness of fibre size-based clusters in gaining mechanistic insight into the relationship between skeletal muscle fibre size and myonuclear content. References Brack AS, Bildsoe H, Hughes SM. (2005), *Journal of Cell Science*, 118: 4813–4821. Mackey AL, Karlsen A, Couppé C, Mikkelsen UR, Nielsen RH, Magnusson SP, Kjaer M. (2014). *Acta Physiologica (Oxford, England)*, 210: 612–627. Contact ak@anderskarlsen.dk

NO RESISTANCE EXERCISE INDUCED MUSCLE PROTEIN SYNTHESIS RESPONSE IN ELDERLY MEN AS COMPARED TO YOUNG

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Introduction Young and elderly do not seem to have different basal muscle protein synthesis (MPS) rates (Volpi et al., 2001), however, elderly has shown diminished MPS responses to both exercise (Kumar et al., 2009) and essential amino acid feeding (Cuthbertson et al.,