with higher τPCr (β = 0.39, p-value <.001) after adjusting for sex, race, height and weight. After including MVPA as an independent variable, the standardized regression coefficient for age was attenuated by 40% to 0.22. p-value <.001). MVPA was strongly associated with lower τPCr (β = -0.33, p-value <.001) after adjusting for health status, education and smoking history and was only attenuated by 3% after additional adjustment for age. These results suggest that MVPA is strongly associated with muscle oxidative capacity independent of age, providing mechanistic insights into the health benefits of daily physical activity in older persons.

HAND2 TRANSCRIPTION FACTOR ENHANCES NMJ ORGANIZATION AND FUNCTION IN OLD MICE

Anna Carolina Zaia Rodrigues,[1] Henry J. Bonilla,[1] Maria Laura Messi,[1] Zhong-Min Wang,[1] Willard M. Freeman,[2] and Osvaldo Delbono[1], *1. Wake Forest University, Winston-Salem, North Carolina, United States, 2. University of Oklahoma Health Science Center, Norman, Oklahoma, United States*

Over time, declining muscle force and power leads to mobility disability and impaired quality of life. In aging rodents and humans, a denervation and reinnervation process is strongly implicated in sarcopenia: the progressive decline of skeletal muscle mass, composition, and function. We propose that the concomitant decline in expression of Hand2, a key transcription factor (TF) for sympathetic neuron maintenance, induces motor pre- and postsynaptic neuromuscular junction (NMJ) instability and disorganization. To counter the deleterious effect of sympathetic denervation, we developed a novel viral vector (AAV9-Hand2-eGFP, Hand2) carrying Hand2 expression exclusively to sympathetic neurons. Male and female, 16-month-old mice, were examined for signs of muscle denervation and sarcopenia 6 months after IV injection with either Hand2 or control empty virus (AAV9-eGFP, EV). We found that Hand2 increased preterminal synaptic vesicle release, neurofilament phosphorylation (Neurite length: Hand2: 3732±496 μm, EV: 2674±165 μm; P <0.01), NMJ pre/postterminal co-localization, hindlimb muscle mass (EDL: 25%, soleus: 14%, tibialis anterior: 17% and gastrocnemius: 25%; n = 6-8 muscles per treatment group; P < 0.01), myofiber cross-sectional area, and protein kinase-A RIIα/RIα ratio (EV, RIIα:1.05±0.03, RIα:0.93±0.04, ratio: 1.13; Hand2, RIIα:1.81±0.03, RIα:0.94±0.03, ratio: 1.94; P<0.001) which contributes to stability of the NMJ. We also examined Hand2 gene methylation, and RNA-sequencing, muscle metabolomics, and whole body and muscle function with aging in EV and Hand2 injected mice. Our data indicate that expression of Hand2 significantly enhances skeletal muscle adrenergic receptor signaling through the canonical pathway, and prevents in NMJ transmission, and muscle mass and function decline with aging.

FRAILTY ASSESSMENT BASED ON THE QUALITY OF DAILY WALKING

Danya Pradeep Kumar,[1] Nima Toosizadeh,[1] Jane Mohler,[1] and Kaveh Laksari[1], *1. Biomedical Engineering, University of Arizona, Tucson, Arizona, United States*

Frailty is an increasingly recognized geriatric syndrome resulting in age-related decline in reserve across multiple physiologic systems. An impaired physical function is a prime indicator of frailty. In this study, we aim to implement a body-worn sensor to characterize the quantity and quality of everyday walking, and establish associations between gait impairment and frailty. Daily physical activity was acquired for 48 hours from 125 older adults (≥65 years; 44 non-frail, 60 pre-frail, and 21 frail based on the Fried gold standard) using a tri-axial accelerometer motion-sensor. Continuous purposeful walks (≥60s) without pauses were identified from time-domain acceleration data. Power spectral density (PSD) analysis was performed to define higher gait variability, which was identified by a shorter and wider PSD peak. Association between frailty and gait parameters was assessed using multivariable nominal logistic models with frailty as the dependent variable, and demographic parameters along with the gait parameters as the independent variables. Stride times, PSD gait variability, and total and maximum continuous purposeful walking duration were significantly different between non-frail and pre-frail/frail groups (p<0.05). Using a step-wise model with the above qualitative and quantitative gait parameters as predictors, the pre-frail/frail group (vs. non-frail) was identified with 71.4% sensitivity and 75.4% specificity. Everyday walking characteristics were found to be accurate determinants of frailty. Along with quantitative measures of physical activity, qualitative measures are critical elements representing the stages of frailty. In-home gait analysis is advantageous over clinical gait analysis as it enables cost- and space-effective continuous monitoring.

LOW-INTENSITY EXERCISE ENHANCES MUSCULAR ANDROGEN/ANDROGEN RECEPTOR TO INHIBIT MYOSTATIN PATHWAY

Bo-Kyung Son,[1] Masato Eto,[1] Miya Oura,[1] and Masahiro Akishita[1], *1. Department of Geriatric Medicine, Graduate School of Medicine, the University of Tokyo, Tokyo, Japan*

Background: Physical exercise is well documented to induce muscle size, strength, and energy metabolism. Although the contribution of systemic or local androgen in exercise-adapted muscle hypertrophy has been suggested, less is known about the molecular pathway of androgen in response to exercise. In the present study, we examined roles of androgen/androgen receptor (AR) after exercise, especially for the suppression of myostatin, a potent negative regulator of muscle mass. Methods and Results: To examine the effects of exercise, we employed low-intensity exercise in mice and electric pulse stimulation (EPS) in C2C12 myotubes. Both mRNA and protein levels of AR significantly increased in skeletal muscle of low-intensity exercised mice and C2C12 myotubes exposed to EPS. Production of testosterone and DHT from EPS-treated C2C12 myotubes was markedly increased. Of interest, we found that myostatin was clearly inhibited by EPS, and its inhibition was significantly abrogated by flutamide, a specific antagonist of AR. Furthermore, IL-6 and phospho-STAT3 (pSTAT3) expression, the downstream pathway of myostatin, were decreased by EPS and this was also reversed by flutamide. Similar downregulation of myostatin and IL-6 was seen in skeletal muscle of low-intensity exercised mice. Conclusion: Muscle AR expression and androgen production were increased by exercise and EPS treatment. As a mechanistical