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Old age generally leads to smaller, weaker and slower skeletal muscles. To address the independent effects of weakness vs. slowing on fatigue in aging, we used a custom ergometer in a whole-body, 3 tesla magnetic resonance system to quantify knee extensor size, torque, velocity, power and intracellular energetics at baseline and during two 4-min fatiguing contraction protocols; one in which contraction velocity was constrained and torque varied (i.e., torque-dependent contractions; isokinetic, IsoK), and one in which torque was constrained and velocity varied (i.e., velocity-dependent contractions; isotonic, IsoT). On separate days, 10 young (27.5±1.2 yrs, 6 men) and 10 older (71.2±1.6 yrs, 5 men) healthy adults completed the IsoK (120°·s⁻¹, 0.5 Hz) and IsoT (20% maximal torque, 0.5 Hz) protocols, with continuous measures of intracellular [Pi], pH, and [H₂PO₄⁻]. At baseline, contractile volume (803.5±72.3 vs. 1,125.6±109.9cm³), specific IsoK torque (0.035±0.004 vs. 0.058±0.007Nm·cm⁻³) and IsoT velocity (121.4±11.6 vs. 176.3±8.0deg·s⁻¹) were greater in young than older (p≤0.023). Fatigue (%initial specific torque) was greater in young than older for IsoK (40.1±3.0 vs. 61.2±5.3%, p=0.0028), and accompanied by greater [Pi] and [H₂PO₄⁻] and lower pH in the young (p≤0.001). For IsoT, fatigue (%initial velocity) was not different between groups (young: 56.5±5.5 vs. older: 47.2±4.9%, p=0.661), despite lower pH and greater [H₂PO₄⁻] in young than old (p≤0.001). Collectively, these results reveal that normalizing dynamometer outputs to assess age-related differences in fatigue obscures baseline differences in muscle weakness. Further, our results suggest the contractile machinery may be less sensitive to changes in pH in older than young.

WHOLE GENOME LINKAGE SCAN IDENTIFIES A NOVEL LOCUS ON 3Q28 FOR TG/HDL-C RATIO CHANGE OVER TIME

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TG/HDL-C ratio (THR) represents a single inherited surrogate predictor of hyperinsulinemia or insulin resistance that is associated with premature aging processes, risk of diabetes and increased mortality. To identify genetic loci for THR change over time (Δ THR), we conducted a whole genome linkage scan among subjects of European ancestry who had complete data from two exams collected about seven years apart from the Long Life Family Study (LLFS, n=3091), a study with familial clustering of exceptional longevity in the US and Denmark. Subjects with diabetes or using medications for dyslipidemia were excluded from this analysis. Δ THR was derived using growth curve modeling, and adjusted for age, sex, PCs, familial membership, and then log-transformed to approximate normality. Our linkage scan was built on haplotype-based IBD estimation with 0.5 cM average spacing. Heritability of Δ THR was moderate

(46%), and evidence for significant linkage (LOD>3) was identified on 3q28 (LOD=4.1). This locus harbors ADIPOQ among several other promising candidate genes. Interestingly, several studies previously reported suggestive evidence of linkage at this locus for relevant traits including adiponectin, dementia, AD and SBP. This linkage signal was not explained by significant GWAS SNPs for LPL or those under the peak (LOD attenuated to 3.7). In conclusion, we found a novel genetic locus on 3q28 for Δ THR in subjects without diabetes selected for exceptional survival and healthy aging. Further query of sequence elements including rare functional and regulatory variants at this locus is underway which may reveal novel insights on insulin resistance mechanisms for aging.

SESSION 3000 (PAPER)

IMPROVING DEMENTIA CARE

CANADIAN CONSENSUS CONFERENCE ON PSYCHOLOGICAL AND NON-PHARMACOLOGICAL INTERVENTIONS FOR DEMENTIA

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Psychological and non-pharmacological interventions that could have a positive effect on outcomes important to persons living with dementia are essential to identify given the the limited efficacy of dementia medications and the diverse needs of persons living. In 2019, for the first time the Canadian Consensus Conference on the Diagnosis and Treatment of Dementia (CCCDDT) created a working group to develop recommendations related to a broad range of psychosocial and non-pharmacological interventions exist, typically aimed at improving cognition, symptoms, or well-being, as well as improving caregiver well-being and coping. The recommendations, primarily intended for primary care physicians, may also allow clinicians, organizations, and communities and help to better meet the needs of people living with dementia and their caregivers. A group of 11 experts, including persons living with dementia and informal caregivers, as well as clinicians and researchers from various organizations both nationally and internationally were invited to participate. A rapid review of meta-analyses and literature reviews on psychological and non-pharmacological interventions was conducted. The synthesized results were submitted for a consensus building approach using a Delphi method, involving a panel of more than 50 Canadian participants. Recommendations with a positive vote of 80% or more were considered to have reached consensus. All proposed recommendations reached consensus using the Delphi process. Details of the recommendations are