

predictors of performance on a proxy version of the Mini-cog, a screening tool for cognitive impairment, assessed at age 60. We additionally tested general cognitive ability assessed at age 50 as a potential mediator of associations between childhood personality and Mini-cog scores. These are some of the first data available to test associations between personality in childhood and cognitive outcomes decades later in adulthood. The sample was comprised of 330 participants (52% women) who completed half day clinic exams at average age 50 and again at age 60. Childhood personality traits were assessed at average age 10 using teacher ratings of personality. General cognitive ability was measured at average age 50 using the Woodcock-Johnson Brief Abilities Inventory (BIA). At age 60, participants completed a clock drawing task and the Hopkins Verbal Learning Task (HVLT-R). These were used to construct a proxy Mini-cog. Partial correlations controlling for age and gender showed that childhood Conscientiousness ($r = -.13$), Intellect/Openness ($r = -.12$), and Agreeableness ($r = .12$) were associated with Mini-cog scores. In path analyses testing age 50 cognitive ability as a mediator of these effects, both childhood Intellect/Openness and Conscientiousness showed indirect effects through age 50 cognitive ability on Mini-cog performance at age 60. Childhood Agreeableness maintained an independent association with Mini-cog scores, not mediated by adult cognitive ability. We discuss possible mechanisms that may account for the observed associations.

SENESCENCE AND APOPTOSIS IN AGING SKELETAL MUSCLE

D. Kwak¹, C.W. Baumann², L.V. Thompson¹, 1. *Physical Therapy and Athletic Training, Boston University, Boston, Massachusetts*, 2. *University of Minnesota, Minneapolis, Minnesota*

In mitotic cells, senescence and apoptosis occur in response to certain stressors (e.g., aging). However, in post-mitotic cells, such as multinucleated skeletal muscle myofibers the extent to which cellular senescence and apoptosis occurs is largely unknown. Therefore, the purpose of this study was to explore the role of senescence and apoptosis as drivers of age-associated sarcopenia. We hypothesized that biomarkers of senescence and apoptosis would increase in aging skeletal myofibers and that these changes would be associated with sarcopenia. To identify biomarkers of senescence and apoptosis, the extensor digitorum longus (EDL) and tibialis anterior (TA) muscles were examined from adult (<12 months, N=11) and elderly (>28 months, N=11) male C57BL/6 mice. The EDL was used to assess ex vivo whole muscle physiology while the TA was used to determine protein content (p53, p21, p16, caspase 3, and IL-6) and presence of SA β -gal and Tunnel via histological staining. Muscle wet weight and absolute force production were significantly reduced in the elderly mice. Aging significantly increased p21, IL-6, and caspase 3 content; however, did not appear to impact p53 nor p16 expression. Myofibers of elderly mice had an increase of apoptotic myonuclei, but only presented a small percentage of SA β -gal. Taken together, biomarkers of cellular senescence and apoptosis are present in muscle of elderly mice. Because p21, IL-6, caspase 3, and apoptotic cells were increased in the elderly muscle it is possible that these pathways contribute to sarcopenia.

NEW EVIDENCE THAT PROTECTIVE EFFECTS OF FAMILIAL LONGEVITY EXPIRE AT OLDER AGES

L.A. Gavrilov¹, N.S. Gavrilova^{1,2}, V.N. Krut'ko², 1. *NORC at the University of Chicago, Chicago, Illinois*, 2. *Federal Research Center "Computer Science and Control" of Russian Academy of Sciences, Moscow, Russian Federation*

This study presents new findings that challenge a common belief in sustained protective effects of familial longevity during the human life course. We found that the survival advantage of biological relatives of long-living individuals vanishes at older ages, suggesting that protective effects of longevity-assurance genes disappear at age 95–100 years. We compared survival patterns of 3,664 siblings of U.S. centenarians with survival of a control group of 4,078 siblings of shorter-lived individuals (died at age 65 years). Survival analysis after age 40 years was conducted separately for 4,201 male and 3,541 female siblings born in 1886–1896. Although siblings of long-lived individuals have lower mortality at younger ages compared to siblings of shorter-lived individuals, their actuarial aging rate (rate of mortality growth with age) is consistently higher, so that their survival advantage practically disappears at older ages. To validate these findings, we analyzed data on survival of 3,408 U.S. centenarians born in 1890–97 with known information on maternal and paternal lifespan. We found that indeed both maternal and paternal longevity (lifespan 90+ years) have no protective effect on survival after age 100 years. These findings challenge predictions of the mutation accumulation theory of aging about higher survival advantage at older ages associated with familial longevity due to lower load of late-acting deleterious mutations. Our findings are compatible with predictions of the reliability theory of aging suggesting higher initial levels of system redundancy (reserves) in individuals with protective familial/genetic background. Supported by the National Institute on Aging (R01 AG028620 to L.G.).

EFFECT OF CHRONIC POLYPHARMACY AND THE DRUG BURDEN INDEX (DBI) ON PHYSICAL FUNCTION IN AGED MICE

J. Mach^{1,2,3}, C. Logan^{1,2}, G. Gemikonakli^{1,2}, A.E. Kane^{4,2}, S.E. Howlett⁴, R. de Cabo⁵, D.G. Le Couteur^{2,6}, S.N. Hillmer^{1,2,3}, 1. *Kolling Institute, Sydney, New South Wales, Australia*, 2. *University of Sydney, Sydney, New South Wales, Australia*, 3. *Royal North Shore Hospital, Sydney, New South Wales, Australia*, 4. *Dalhousie University, Halifax, Nova Scotia, Canada*, 5. *National Institute on Aging, Baltimore, Maryland*, 6. *Concord Hospital, Sydney, New South Wales, Australia*

Increasing DBI (measure of patient's total exposure to anticholinergics and sedatives) is associated with impaired physical function in observational studies of older adults. We aim to determine the effect of polypharmacy (use of ≥ 5 drugs) and increasing DBI on functional outcomes in aged mice. From 12 to 21 months of age male C57BL/6 mice are fed control diet or treated feed/water containing therapeutic doses of five drugs with Zero DBI (simvastatin, metoprolol, omeprazole, paracetamol, irbesartan), Low DBI (simvastatin, metoprolol, omeprazole, paracetamol, citalopram), High DBI (simvastatin, metoprolol, oxybutynin, oxycodone, citalopram), or single drug (simvastatin, metoprolol, oxybutynin, oxycodone or citalopram). A panel of functional tests