Recent data has shown a consistent but modest association between hearing impairment and poor mobility; both are strongly associated with cognition. Cognitive function may moderate the relationship between hearing and mobility. We analyzed 601 cognitively normal older participants from the Baltimore Longitudinal Study of Aging who had concurrent data on cognition (attention, executive function, sensorimotor function), hearing (pure-tone average, PTA), and mobility (6-meter gait speed, 400-meter time). We performed multivariable-adjusted linear regression to test two-way interactions between each cognitive measure and PTA. There were significant PTA interactions with all cognitive measures on 400-meter time. There was a significant interaction between PTA and sensorimotor function on 6-meter gait speed. Among cognitively normal older adults, poorer hearing is more strongly associated with poor mobility in those with low cognition, especially sensorimotor function. Future studies are needed to understand how cognition may moderate the relationship of hearing impairment with mobility decline over time.

Session 2110 (Symposium)

MOLECULAR RESILIENCY AND AGING
Chair: Adam Salmon

Resilience is described as the ability to respond to acute forms of stress and recover to normal homeostasis. There is growing evidence that biology of resilience is entwined with the biology of aging. With increasing age, resilience decreases and is a likely contributor to increased morbidity, frailty and susceptibility to death with age. Conversely, increased resilience across numerous physiological markers of function is associated with longevity and healthy aging. The variation in resilience in populations suggests biological and molecular regulatory mechanisms that might provide insight into interventions to improve resilience, healthy aging and longevity. In this session, speakers will provide insight regarding short-term assays of resilience in animal models that prove useful both in delineating these biological mechanisms as well as inform on potential translational models to better understand biological resilience in human populations. The sessions focus is on defining these assays and discussion of the biological relevance each resilience assay in terms of the regulation of aging. The goals of these studies range from identifying potential predictors of individual lifespan within markers of functional resilience to leveraging geroscience to define whether markers of resilience can be modified through interventions to the aging process. Moreover, better understanding of the biology of resilience could assist in defining novel interventions that improve resilience and thereby enhance longevity.

CELLULAR RESILIENCE AS A POTENTIAL PREDICTOR OF LIFESPAN
Adam Salmon, *University of Texas Health San Antonio, San Antonio, Texas, United States*

The progressive decline of resilience during the aging process across multiple functional systems suggests basic biological mechanisms of regulation. We exploited a primary cell model to identify markers of cellular resilience or the ability of cells in culture to respond and return to homeostasis following acute challenge including metabolic, oxidative, or proteostatic stress. Using primary fibroblasts from minimally-invasive skin biopsies of genetically heterogeneous mice, we are able to determine individual cellular resilience as well as the normal lifespan and healthspan of each donor. Our studies suggest donor age and sex affect cellular resilience and that this measure of resilience can predict functional outcomes in some interventional studies. While longevity studies continue, these studies point to a potential highly important marker of healthspan and longevity as well as a model to delineate the biology of resilience in animal and translational models.

RESILIENCE AS A DETERMINANT OF HEALTHSPAN AND LIFESPAN IN MICE
Nathan LeBrasseur, *Mayo Clinic, Rochester, Minnesota, United States*

Dynamic measures of physical resilience—the ability to resist and recover from a challenge—may be informative of biological age far prior to overt manifestations such as age-related diseases and geriatric syndromes (i.e., frailty). If true, physical resilience at younger or middle ages may be predictive of future healthspan and lifespan, and provide a unique paradigm in which interventions targeting the fundamental biology of aging can be tested. This seminar will discuss research on the development of clinically relevant measures of physical resilience in mice, including anesthesia, surgery, and cytotoxic drugs. It will further highlight how these measures compare between young, middle-aged, and older mice, and how mid-life resilience relates to later-life healthspan and even lifespan. Finally, it will provide insight into whether interventions targeting the biology of aging can modify physical resilience in mice.

ROLE OF PHYSIOLOGICAL RESILIENCE IN AGING: CHALLENGES AND OPPORTUNITIES
Derek Huffman, *Albert Einstein College of Medicine, Bronx, New York, United States*

Lifespan and healthspan remain a cornerstone of documenting efficacy in aging research. However, it is becoming increasingly appreciated that housing rodents in conventional, unprovoked conditions, rather than exposed to the same variety of stressors normally encountered by free-living humans, has limited our understanding of how these strategies can be translated. Resilience can be defined as the ability of an organism to respond to a physical challenge or stress and return to homeostasis. Indeed, physiologic resilience is recognized to decline with age from a weakening of interactions among multiple physiologic regulatory functions. Here, we have attempted to optimize stress assays as a means of measuring physiologic resilience in mice. Our data demonstrate that these assays can readily detect age-related deficits in recovery, are amendable to geroprotector strategies, including rapamycin, while acute exposure to a stress can accelerate aging and mortality, thereby serving as a potentially useful paradigm for testing age-delaying interventions.

GENETIC VARIANTS CORRELATE WITH BETTER PROCESSING SPEED
Anastasia Gurinovich,[1] Kaare Christensen,[2] Marianne Nygaard,[2] Jonas Mengel-From,[2] Stacy Andersen,[3] Thomas Perls,[1] Paola Sebastiani,[4] and

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Some cognitive abilities, such as vocabulary, are resilient to brain aging, while others such as conceptual reasoning, memory, and processing speed, decline with age and their rate of decline is genetically regulated. Despite the strong genetic heritability of processing speed assessed by the digit symbol substitution test (DSST), previous studies have failed to identify robust common genetic variants associated with this test. The Long Life Family Study (LLFS) includes long lived individuals and their family members who maintain good DSST scores as they age and who may carry variants associated with better DSST. We therefore conducted a genome-wide association study (GWAS) of DSST in LLFS using ~15M genetic variants imputed to the HRC panel of 64,940 haplotypes with 39,635,008 sites and replicated the findings using genetic data imputed to the 1000 Genomes phase 3 reference panel combining two Danish cohorts: the Middle Aged Danish Twins and the Longitudinal Study of Aging Danish Twins. The GWAS in LLFS discovered 20 rare genetic variants reaching genome-wide significance (p-value < 5x10-8), including 18 variants associated with better processing speed with large effect size. The genetic associations of rs7623455, rs9821776, rs9821587, rs78704059 in chromosome 3 were replicated in the combined Danish cohort. These genetic variants tagged two hormone receptor related genes, THRB and RARB, both related to cognitive aging. Further gene-based tests in LLFS confirmed that these two genes have protective variants associated with better processing speed.

Session 2115 (Paper)

MORBIDITY, MORTALITY, AND AGING

CREATION AND VALIDATION OF A POLYSOCIAL SCORE FOR MORTALITY AMONG COMMUNITY-DWELLING OLDER ADULTS IN THE UNITED STATES

Yongjing Ping,[1] Chenkai Wu,[1] Michelle Odden,[2] Robert Stawski,[3] and Hoda Magid,[4] *1. Duke Kunshan University, Kunshan, Jiangsu, China (People's Republic), 2. Stanford University, Stanford, California, United States, 3. Oregon State University, Corvallis, Oregon, United States, 4. Stanford University, Stanford University, California, United States*

The interrelatedness between social determinants of health impedes researchers to identify important social factors for health investment. Since the older population had highly diverse social backgrounds, a new approach is needed to quantify the aggregate effect of social factors and develop person-centered social interventions. Participants ([n = 7383], 54.5% female) were aged 65 years or above who complete an additional psychosocial questionnaire in the Health and Retirement Study (HRS) at study entry in 2006 or 2008. Social determinants of health encompassing five social domains: economic stability, neighborhood and physical environment, education, community and social context, and health care system. Five-year mortality was calculated as the number of years from the interview date to the death date. We used the forward stepwise logistic regression to construct the polysocial score and multivariate logistic regressions to assess the associations between polysocial score and five-year mortality. Polysocial score (range: 7 to 59, mean±SD: 35.5±7.5) was created using 15 social determinants of health. Of the 7383 participants, 491 (30.8%), 599 (17.2%), and 166 (7.8%) deaths occurred over five years among participants with a low (0-29), intermediate (30-39), and high (40+) polysocial score, respectively. Participants with an intermediate (Odds Ratio [OR]=0.76; 95% CI, 0.65-0.89) or high (OR=0.46; 95% CI, 0.36-0.59) polysocial score had higher odds of death than those in the low category in the fully adjusted model, respectively. The polysocial approach may offer possible solutions to monitor social environments and suggestions for older adults to improve their social status for specific health outcomes.

EPIDEMIOLOGIC DETERMINANTS OF DYNAMICS IN HEART FAILURE PREVALENCE AND MORTALITY IN OLDER U.S. ADULTS

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Recent declines in heart failure (HF) prevalence and increases in mortality among older adults in the US suggest the need for research to investigate the relative contribution of the epidemiological determinants of these two processes to their historical and current trends. Study data were derived from a 5% sample of Medicare beneficiaries, 1991-2017. Partitioning analysis was used to decompose age-adjusted prevalence and incidence-based mortality (IBM) into their constituent components. HF prevalence trend decomposition demonstrated three phases: (a) Decelerated Increasing Prevalence (1994-2006) mainly driven by decreasing incidence, overpowering increasing survival, (b) Accelerated Declining Prevalence (2007-2014) and (c) Decelerated Declining Prevalence (2015-2017), mainly driven by declining incidence, overpowering declining survival. For HF IBM four phases were identified: (a) Decelerated Increasing Mortality (1994-2001) with declining incidence and increasing survival driving deceleration, (b) Accelerated Declining Mortality (2002-2012), (c) Decelerated Declining Mortality (2013-2016), mainly driven by declining incidence, overpowering declining survival, and (d) Accelerated Increasing Mortality (2017) mainly driven by declining survival, overpowering declining incidence. Study findings suggest that the recent decade-long decline in HF prevalence and 15-year decline in HF mortality mainly reflected decreasing incidence, while the most recent increase in mortality was due to declining survival, which may be associated with the Hospital Readmission Reduction Program. If current trends of incidence and survival persist, HF prevalence and mortality are forecasted to grow, suggesting that actions to reduce HF risk factors and improve treatment and management of HF after diagnosis are warranted.