ASSOCIATION BETWEEN DUAL-TASK GAIT AND COGNITIVE FUNCTION IN OLDER ADULTS

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Community mobility involves walking with physical and cognitive challenges. In older adults (N=116; results here from initial analyses: N=29, Age=75±5 years, 51% females), we assessed gait speed and smoothness (harmonic-ratio) while walking on even and uneven surfaces, with or without an alternate alphabeting dual-task (ABC). ANOVA assessed surface and dual-task effects; Pearson correlations compared gait with global cognition and executive function composite z-scores. The four conditions (even, uneven, even-ABC and uneven-ABC) affected speed(m/s) (0.97±0.14 vs 0.90±0.15 vs 0.83±0.17 vs 0.79±0.16). Smoothness (2.19±0.48 vs 1.89±0.38 vs 1.92±0.53 vs 1.7±0.43) was affected by only surface (controlled for speed). Greater speed was associated with better global cognition(ρ=0.47 to 0.49, $p<0.05$) for all conditions and with better executive function for even-ABC(ρ=0.39, p=0.04) and uneven-ABC(ρ=0.40, p=0.03). Executive function was associated with smoothness during even(ρp=-0.42, p=0.03) and uneven(ρp=-0.39, p=0.04) walking. Type of walking challenge differentially affects gait quality and associations with cognitive function.

COGNITION MODERATES THE RELATIONSHIP BETWEEN HEARING AND MOBILITY IN COGNITIVELY NORMAL OLDER ADULTS

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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

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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

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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

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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

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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

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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.