Older adults with slow gait have a modestly elevated risk of Alzheimer’s disease (AD). Whether strategies to maintain function, such as interlacing periods of activity and rest, modify this relationship is unknown. We analyzed 577 initially cognitively normal participants aged 50+ (53% women, 26% Black) who had baseline data on gait speed and fractionation via ActiHeart. Diagnoses of mild cognitive impairment (MCI)/AD were adjudicated during an average 7.3 years follow-up. We examined gait speed, fractionation, and their interaction with MCI/AD risk using Cox proportional-hazards models, adjusted for demographics and APOE-e4. Each 0.2 m/sec faster gait speed was associated with 24% lower risk of MCI/AD (p=0.04). Fractionation was not associated with MCI/AD risk (p>0.05). There was a significant gait*fractionation interaction (p=0.013). At high fractionation, gait was not predictive of MCI/AD. Slow gait speed is less predictive of future MCI/AD in individuals who fractionate their activity to maintain function, possibly indicating brain function that drives such compensatory strategy is still conserved.

**MILD PARKINSONIAN SIGNS ARE RELATED TO LOWER CORTICO-STRIATAL CONNECTIVITY IN EXECUTIVE NETWORKS**

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Mild Parkinsonian signs (MPS) affect up to 24% of community-dwelling older adults. We hypothesize that MPS are associated with Parkinson’s-like alterations of functional connectivity (FC) in sensorimotor, executive, and reward cortico-striatal networks. Participants (N=266; mean age=83; 57% female) without Parkinson’s completed resting-state fMRI and Unified Parkinson Disease Rating Scale (UPDRS). FC between striatum and cortex was measured within each network. Logistic regression tested associations of each network’s FC with MPS (UPDRS≥0), adjusted for MPS risk factors, then including white matter hyperintensities (WMH). MPS was associated with lower cortical-striatal FC in the left executive cortico-striatal network (OR [95% CI]: 0.188 [0.043, 0.824]). Association survived adjusting for risk factors (OR [95% CI]: 0.162 [0.030, 0.874]) but was attenuated after including WMH (0.209 [0.036, 1.200]). In stratified analyses, left executive cortico-striatal FC was associated with MPS only for those with higher WMH (0.077 [0.010, 0.599]). Future work should examine whether higher FC protects against the influence of WMH on MPS.

**MOTOR SKILL TRAINING EFFECT ON REAL-TIME PREFRONTAL CORTEX ACTIVATION DURING WALKING**

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We aimed to test the effects of motor skill training (MST) on gait automaticity measured by changes in prefrontal cortex (PFC) activation during actual walking. We used data from a 12-week trial of older adults (mean age=75.5, 60.5% women) randomized to standard physical therapy and standard+MST in a 1:1 ratio. Functional near infrared spectroscopy (fNIRS) measured PFC activation during simple and dual task walking. We will apply linear mixed models to assess effects of task, time, and MST on PFC activation. We will compare the PFC activation 1) during dual task walking compared to simple walking; 2) across visits after intervention; and 3) between participants receiving MST compared to standard physical therapy. These results will demonstrate whether gait automaticity, as evidenced by PFC activation during walking, is affected by MST.

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

Jessie VanSwearingen, 1 Mark Redfern, 2 Ervin Sejdic, 2 Andrea Rosso, 1 and Anisha Suri, 1 1 School of Health and Rehabilitation Sciences, Pittsburgh, Pennsylvania, United States, 2 Swanson School of Engineering, University of Pittsburgh, Pittsburgh, Pennsylvania, United States, 3 University of Pittsburgh, Pittsburgh, Pennsylvania, United States

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 (p=0.47 to 0.49, p<0.05) for all conditions and with better executive function for even-ABC (p=0.39, p=0.04) and uneven-ABC (p=0.40, p=0.03). Executive function was associated with smoothness during even (p=0.42, p=0.03) and uneven (p<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**

Brent Small, 1 Jennifer Deal, 2 Nicole Armstrong, 3 Susan Resnick, 4 Frank Lin, 5 Luigi Ferrucci, 4 Qu Tian, 4 and Daniel Pupo, 4 1 University of South Florida, Tampa, Florida, United States, 2 Johns Hopkins University, Baltimore, Maryland, United States, 3 Warren Alpert Medical School of Brown University, Providence, Rhode Island, United States, 4 National Institute on Aging, Baltimore, Maryland, United States, 5 Johns Hopkins University, Johns Hopkins University, Maryland, United States, 6 University of South Florida, University of South Florida, Florida, United States

GSA 2021 Annual Scientific Meeting
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 informing on potential translational models to better understand biological resilience in human populations. The sessions focus on defining these assays and discussion of the biological relevance each 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 RESILIENCY 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 session 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 RESILIENCY 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,2 Thomas Perls,1 Paola Sebastiani,4 and