THE EFFECTS OF AGE-BASED EVALUATIONS ON OLDER ADULTS' GAIT VARIABILITY

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Older adults are stereotyped as being slow, weak, and frail. In this study we examined how these stereotypes about age-related physical decline affect older adults' walking performance. Healthy, community-dwelling older adults were asked to walk at their own comfortable pace along a 24' temporospatial-measuring walkway 10 times. For some participants this was done with a normal-base of support (i.e., usual gait). However, for other participants this was done with a narrow-base of support (i.e., walking within a path of 15 cm outlined by tape). Walking tasks were done either in the presence or absence of a negative age-based evaluation. Results showed that the negative age-based evaluations were associated with greater stride-to-stride variability, particularly for participants who felt less confident in their abilities. Given that gait variability is a predictor of falling, this raises the possibility that negative age-based evaluations can produce concerns that are an intrinsic risk factor for falls.

SESSION 3385 (SYMPOSIUM)

CELL NON-AUTONOMOUS MECHANISMS OF AGING

Chair: Scott Leiser, *University of Michigan, Ann Arbor, Michigan, United States*

It is now recognized that biological aging can be affected both positively and negatively by intercellular communication. This symposium will focus on recent discoveries related to cell non-autonomous mechanisms of aging.

CELL NON-AUTONOMOUS SEROTONIN SIGNALING MEDIATES STRESS RESISTANCE AND LONGEVITY

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The ability of organisms to perceive and respond to their environment is crucial to their long-term survival. Recent studies in model organisms identify signaling pathways that perceive environmental stress and cell non-autonomously modify systemic physiology. These pathways often originate in the neurons, where key cells monitor the external environment for changes including food availability, air-quality, and the presence of dangerous toxins. Our previous work identified a key role for serotonin signaling in the induction of flavin-containing monooxygenase-2 (fmo-2) downstream of hypoxic signaling. fmo-2 expression is necessary and sufficient to promote stress resistance and longevity downstream of multiple genetic pathways, making it a useful tool for identifying key components of these pathways. Our current data defines environments, pathways, and signaling molecules that induce fmo-2 and subsequently increase lifespan. Our resulting data define key roles for serotonin signaling and fmo-2 that rely upon the perception of oxygen and food.

NEURONAL FGF-21 SIGNALING: A SENSOR OF DIETARY PROTEIN

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Our data demonstrates that dietary protein restriction increases energy expenditure and improves glucose homeostasis, and that this effect is largely mediated by the metabolic hormone fibroblast growth factor 21(FGF21). Considering that the central nervous system (CNS) is acknowledged as a major regulator of both energy and glucose homeostasis, we have extended our studies to identify the tissue site mediating these FGF21-dependent effects via dietary protein restriction. In this study, mice with dysfunctional FGF21-signaling in either the CNS or adipose tissue were fed a control or low protein (LP)-diet to assess changes in body weight and metabolic endpoints. Our data show that LP diet increased energy expenditure and reduced body weight in control littermates, but these effects were lost in mice bearing CNS-specific deletion of Klb. These data highlight a liver to brain FGF21-signal as the first known neuroendocrine mechanism to explain the coordinated metabolic changes induced by dietary protein restriction.

INCREASE IN HSP25 EXTENDS LIFESPAN AND IMPROVES RESPONSE TO TAU TOXICITY THROUGH A CELL, NON-AUTONOMOUS MECHANISM

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The accrual of aggregation-prone cytotoxic proteins underlies neural pathologies seen in aging, Alzheimer's disease and other dementias. Recent evidence indicates that heat shock protein 25kDa (HSP25) interacts with tau. To demonstrate a causal role for HSP25 in these pathologies, we overexpressed HSP25 protein in worms. This manipulation led to an increase in life span. Moreover, the longevity-effect was associated with increased expression of genes downstream of the SKN-1/Nrf2 stress-response transcription factor. HSP25 over-expression also reduces aggregate pathology and extends lifespan in a C. elegans neuronal-specific, aggregate-prone tau model . We propose that over-expression of HSP25 could provide protection from protein aggregation induced neurodegeneration. However, it is not yet clear whether this HSP25 effect could be efficaciously provided exogenously by other cell types. Thus, we will test whether increased peripheral HSP25 will reduce protein aggregation and stimulate a global Skn-1 stress-response pathway, reduce toxicity in neurons, and improve health outcomes.

RESTORATION OF HYPOXIA SIGNALING IMPROVES AGING-ASSOCIATED LOSS OF SKELETAL MUSCLE REGENERATIVE POTENTIAL

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Idranil Sinha[1]

Skeletal muscle retains the ability to regenerate throughout life, but this decreases significantly with aging.