respectively]. Both positive behaviors and higher age 20 GCA were associated with less brain aging. The GCA-lifestyle interaction was also significant. Those with both lower age 20 GCA and fewer positive behaviors had older brains relative to chronological age [F=5.00; p=. 03]. When GCA was high, however, participants had younger brains, regardless of lifestyle behaviors, suggesting a protective effect of early high GCA or cognitive reserve on later brain health. However, for those with lower cognitive reserve, positive lifestyle behaviors appeared to be protective against brain aging nearly three decades later. Results highlight the important role of cognitive reserve and lifestyle factors for later life brain health.

AGING RELATED TRANSCRIPTOMIC CHANGES IN THE MOUSE MODELS OF ALZHEIMER'S DISEASE

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Alzheimer's Disease (AD) is characterized by multiple clinical phenotypes and molecular signatures at different stages of the disease and aging is the major risk factor for sporadic AD. Aging and AD are linked at molecular, cellular and systems level with commonalities in inflammation and associated immune response in the brain. Mouse models of AD were developed that mimic various aspects of aging-associated neurodegeneration and inflammation. Research in mouse models of AD showed that drugs and treatments designed for AD can decelerate aging phenotypes suggesting efficient utilization of these models in aging research. We analyzed RNA-Seq transcriptomic data from transgenic mouse models of familial AD (APP/PS1 and 5XFAD) and knock-in mouse models of late-onset AD (APOE and TREM2) at the ages between 4-months and 24-months. The number of differentially expressed genes between transgenic/knock-in and WT mice increased by age in all mouse models. Gene set enrichment analysis identified metabolic pathways, including oxidative phosphorylation, altered in an age and genotype related manner in the brain of APP/PS1 and 5XFAD mice that recapitulate major features of amyloid pathology. Immunity related pathways were enriched in APOE4 model carrying Trem2*R47H mutation at >12 months-old. We also mapped the transcriptional signatures to co-expression gene modules of human LOAD from the AMP-AD consortium and observed correlations specific to each mouse model. Our study provides a detailed view of how the aging interacts with AD-relevant pathologies at the transcriptome level and demonstrates potential translational relevance of the AD mouse models in the context of human aging.

ALZHEIMER'S DISEASE-ASSOCIATED PATHOLOGY IN A TRANSGENIC MOUSE MODEL RESULTS IN ALTERED VOIDING FUNCTION

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Alzheimer's disease (AD) is a devastating disorder primarily affecting older adults and is the most common neurodegenerative disease in the US. More than one in three AD patients experience AD-associated urinary dysfunction (ADUD), which directly contributes to their institutionalization. While ADUD has been clinically regarded as a result of poor cognitive control over urinary function, the physiology underlying loss of urinary control remains unknown. We hypothesize that beta-amyloidosis in the CNS results in pathologic changes in urinary structure and function. Male and female Tg-APP/PS1DE9 mice were used before plaque deposition (4-6 months) and after plaque accumulation (8-10 months) and compared to their WT littermates. Pressure-flow cystometry was conducted under urethane anesthesia to assess urinary performance at the level of the autonomic nervous system in the absence of cortical control. Pharmacomyography was performed on bladder strips to determine tissue-level changes in the absence of CNS input. In Tg-APP/PS1DE9 mice, plaque accumulation resulted in diminished volume sensitivity and decreased voiding efficiency. Pharmacologic studies showed aberrant drug responses, altered cholinergic signaling, and decreased resilience of tissue longevity after plaque accumulation. Based on our findings, we conclude that the AD-related pathology of Aβ accumulation results in a distinct urinary phenotype in our model, analogous to the ADUD observed in AD patients. Establishing and expanding models of ADUD to other mouse models of AD-associated pathology may improve the efficacy of treating ADUD and increase quality of life for patients and their caregivers.

CAROTID REVASCULARIZATION IMPROVES BALANCE AND MOBILITY, PARTICULARLY IN PATIENTS THAT ARE MOST IMPAIRED

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Balance and mobility function worsen with age, and more so for those with underlying diseases. Our research has demonstrated that asymptomatic carotid artery stenosis (ACAS) is associated with worse balance and mobility, and a higher fall risk, compared to older adults with similar comorbidities, but without ACAS. Thus, ACAS, with attendant blood flow-restriction to the brain is a potentially modifiable risk factor for balance and mobility dysfunction. The purpose of this study was to evaluate the impact of restoring blood flow to the brain by carotid revascularization, on balance and mobility in patients with high-grade ACAS (≥70% diameter-reducing stenosis). Twenty adults (67.0±9.4 years) undergoing carotid revascularization for high-grade stenosis were enrolled. A balance and mobility assessment was performed before- and six weeks- after carotid revascularization and included: Short Physical Performance Battery (SPPB), Berg Balance Scale (BBS), Four Square Step Test (FSST), Dynamic Gait Index (DGI) Timed Up and Go (TUG), gait speed, MiniBESTest, and Walk While Talk (WWT) test. Paired t-tests assessed changes in outcome measures between the two-time points. Significant improvements were observed in measures that combined walking with dynamic movements, DGI (P=0.003), and MiniBESTest