three groups. Dual decliners experience faster decline in visuospatial ability, greater atrophy in selected motor areas, and greater increase in depressive symptoms, suggesting potential mechanisms underlying increased dementia risk in dual decliners.

MULTIMODAL NEUROIMAGING PREDICTORS OF GAIT DECLINE

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Prior studies suggesting associations between cortical brain areas and gait speed has been largely cross-sectional and limited to one modality neuroimaging. Using machine learning from 506 cognitively normal BLSA participants aged 55+ who had repeated measures of brain volumes, diffusion tensor imaging (DTI), and gait speed, we examined multimodal neuroimaging predictors of gait decline, accounting for demographics, body composition, and grip strength. Significant predictors of gait decline included changes in volumes and DTI measures of gray matter in selected frontal, parietal, temporal, and subcortical areas, as well as white matter changes in both fractional anisotropy and diffusivity of tracts connecting frontal areas to subcortical motor areas. This predictive model highlights the importance of atrophy and microstructural deterioration in selected frontal and subcortical motor areas in predicting gait speed decline.

MEDIAL TEMPORAL TAU PATHOLOGY IS ASSOCIATED WITH VERBAL MEMORY

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Medial temporal tau pathology is frequently observed in individuals over 70 regardless of cognitive status. To understand the link between tau and cognitive performance, we evaluated tau pathology using 18F-flortaucipir positron emission tomography among 95 cognitively normal participants from the Baltimore Longitudinal Study of Aging. We examined tau levels in early Braak regions (entorhinal cortex and hippocampus) in relation to verbal episodic memory performance concurrent with and prior to the tau scan using linear mixed effects models adjusted for age, sex, amyloid status, and time from PET scan. Higher hippocampal tau burden had a trend-level association with lower concurrent memory performance ($p=0.05$). Greater tau pathology in the hippocampus and entorhinal cortex was associated with steeper decline in memory performance prior to tau scan ($p=0.013$ and 0.026, respectively). These findings suggest that therapeutic interventions targeting tau pathology may need to be administered early among cognitively normal individuals to prevent memory decline.

CEREBRAL MICROSTRUCTURE IN AGING USING ADVANCED QUANTITATIVE MRI

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White matter (WM) maintenance through oligodendrocyte metabolism is an energy-intensive process. Myelin homeostasis is sensitive to hypoxia, ischemia, or hypoperfusion. Besides substrate delivery, adequate cerebral blood flow (CBF) is crucial for removal of metabolic byproducts such as iron. While some data show decreased myelin content and CBF with aging, the association between CBF and myelination is unknown. Further, breakdown of oligodendrocyte and iron may potentiate myelin loss through oxidative mechanisms. Whether iron deposition is related to myelination is unclear. Using advanced MRI methodology, we investigated associations between CBF deficits, myelin loss, and iron deposition in cognitively normal individuals. We found significant association between i) CBF deficits and myelin loss (N=67,age24-88), ii) myelin loss and iron accumulation (N=92,age21-94), and iii) CBF deficits and iron accumulation (N=35,age22-88) in critical brain structures. This work may lay the foundation for further investigations of age-related WM degeneration and markers to differentiate normal from abnormal alterations.

BILE ACIDS IN DEMENTIA: BRAIN AMYLOID, WHITE MATTER LESIONS, AND ATROPHY

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While Alzheimer's disease (AD) and vascular dementia (VaD) may be accelerated by hypercholesterolemia, the mechanisms underlying this association is unclear. Using a novel, 3-step study design we examined the role of cholesterol catabolism in dementia by testing whether 1) the synthesis of the primary cholesterol breakdown products (bile acids (BA)) were associated with neuroimaging markers of dementia; 2) pharmacological modulation of BAs alters dementia risk; and 3) brain BA concentrations and gene expression were associated with AD. We found that higher serum concentrations of BAs are associated with lower brain amyloid deposition, slower WML accumulation, and slower brain atrophy in males. Opposite effects were observed in females. Modulation of BA levels alters risk of incident VaD in males. Altered brain BA signaling at the metabolite and gene expression levels occurs in AD. Dysregulation of peripheral cholesterol catabolism and BA synthesis may impact dementia pathogenesis through signaling pathways in the brain.