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Alzheimer's disease (AD) is the most common cause of dementia in the old adult population. AD pathogenesis has been linked to the aggregation of toxic proteins, e.g., amyloid-β and tau. The glymphatic system may play an important role in clearing out these proteins via cerebrospinal fluid (CSF) flows through perivascular and interstitial spaces. Recent studies have suggested low-frequency (<0.1 Hz), sleep-dependent global blood-oxygenation-dependent-level (gBOLD; global resting-state functional MRI signal) during resting state is coupled with CSF movements, suggesting their potential link to glymphatic function. Here, we directly investigated whether the coupling between the gBOLD and CSF signals is related to AD-related pathology. By analyzing neuroimaging, neurobiological, and neuropsychological data from 118 human subjects (58-90 years of age; AD, early-stage AD, and control subjects included) collected in the Alzheimer's Disease Neuroimaging Initiative project, we found a strong coupling between the gBOLD and CSF signals. More importantly, the strength of this gBOLD-CSF coupling was significantly correlated with cortical amyloid-β level ($p = 0.019$), cognitive decline in the subsequent two years ($p = 0.013$), disease severity ($p = 0.035$), and several AD-related risk factors, including aging ($p = 0.011$), and gender ($p = 0.026$). These findings provide initial evidence for the critical role of resting-state low-frequency (<0.1 Hz) neural/physiological dynamics in AD pathology. They also suggest that the gBOLD-CSF coupling may serve as a non-invasive imaging marker for gauging the glymphatic function.

LOCAL ATROPHY OBSERVED IN SUBJECTIVE COGNITIVE DECLINE VARIES BASED ON QUESTIONNAIRE EMPLOYED IN ADNI

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Background: Subjective cognitive decline (SCD) may be associated with increased risk for Alzheimer's disease. However, neither research nor clinical practices have implemented a universal approach to operationalize SCD. This study was designed to determine whether four different methods of defining SCD influence atrophy differences observed between SCD and normal controls (NC). Methods: We included MRI scans from 273 participants (NC and SCD) from the Alzheimer's Disease Neuroimaging Initiative. We used four methods to operationalize SCD: Cognitive Change Index (CCI), Everyday Cognition Scale (ECog), Worry, and ECog+Worry. Deformation-based morphometry was performed to examine volumetric change at the lateral ventricles, amygdala, and superior temporal regions (CerebrA atlas; Manera et al., 2020)). A previously validated MRI analysis method (SNIPE) was used for volume and grading of the hippocampus and entorhinal cortex (Coupe et al., 2012). A logistic regression was completed to examine the association between diagnosis and atrophy in SCD and NC. Results: Left hippocampal grading was lower in SCD than NC with the CCI ($p=.041$) and Worry ($p=.021$). When using ECog+Worry, smaller left entorhinal volume was observed in SCD than NC ($p=.025$). Both the right ($p=.008$) and left ($p=.003$) superior temporal regions were smaller in SCD than NC, with only the ECog. Conclusion: Although SCD questionnaires are designed to measure the same construct, the results here suggest otherwise. These results suggest that the SCD questionnaire employed will influence whether atrophy is observed in SCD relative to NC. Future research is warranted to better understand how different methodologies result in inconsistent findings.

OBESE BODY MASS INDEX IN LATE-LIFE AS A PROTECTIVE FACTOR FOR MILD COGNITIVE IMPAIRMENT, DEMENTIA AND DEATH

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Objective The goal of the current study was to estimate the hazards of conversion from unimpaired to mild cognitive impairment (MCI) to probable dementia and death for underweight, normal, overweight and obese older adults in an aging cohort where the timing of examinations may be associated with the severity of dementia. Methods We analyzed six waves of the National Health and Aging Trends Study (NHATS); a longitudinal aging cohort. Participants were classified into mutually exclusive cognitive statuses: cognitively unimpaired, MCI, probable dementia and death. Time-to-event ratios and cognitive transitions were examined with multistate survival models accounting for misclassification. BMI was computed from height and weight measurements and expressed in kg/m2 and categorized into underweight, normal, overweight and obese. Results Participants (n=6,078) were 77 years old, on average, and the majority were white, females and high school graduates. About one third (32.68%) of the sample has normal BMI, one third is overweight (35.59%), the rests are obese (26.41%) or underweight (5.33%). After adjusting for the effects of diabetes, CVD, vigorous physical activity, age and race/ethnicity, the protective effect of obesity in late-life against developing dementia (HR=0.44; 95%CI[0.29-0.67]) and dying from dementia (HR=0.63; 95%CI[0.42-0.95). Discussion Prior research shows the risk of dementia associated with obesity at older ages is either attenuated or reversed. Our findings support a protective factor of obesity in late-life against conversion to dementia and death.

PDE4D AND HCN1 ULTRASTRUCTURE IN RHESUS MACAQUE ENTORHINAL CORTEX: RELEVANCE FOR AGING AND ALZHEIMER'S DISEASE

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