Cognitive Reserve Modifies Age-Related Alterations in CSF Biomarkers of Alzheimer’s Disease

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BACKGROUND

- Advancing age is the strongest risk factor for both the development of symptomatic Alzheimer’s disease (AD) and the accumulation of AD-related pathophysiological abnormalities
- There is often discontinuity between the presence of AD-related pathology and the emergence of clinical symptoms
- Individual differences in susceptibility to age-related alterations in AD biomarkers, such as cerebrospinal fluid (CSF) amyloid-β(Aβ42), total tau (t-tau), and phosphorylated tau (p-tau)
- Cognitive reserve (CR) has been posited as an explanation for this mismatch

OBJECTIVE

- To investigate whether CR modifies age-related alterations in CSF biomarkers of AD

METHODS

Participants:
- Three hundred and six individuals from the Wisconsin Registry for Alzheimer’s Prevention and the Wisconsin Alzheimer’s Disease Research Center
- Clinically characterized as either cognitively normal (n=249) or cognitively impaired (n=57)
- Cognitively impaired participants had a diagnosis of either mild cognitive impairment (n=16) or Alzheimer’s dementia (n=41)
- CR was indexed by years of education

Data Collection:
- Participants underwent lumbar puncture for collection of CSF samples, from which Aβ42, t-tau, and p-tau were immunoassayed
- Using this data, we additionally computed t-tau/Aβ42 and p-tau/Aβ42 ratios

Statistical Analysis:
- Linear regression included terms for
  - CR
  - Age
  - Sex
  - Apolipoprotein E4 (APOE4) genotype
  - Cognitive status (i.e., cognitively normal vs. cognitively impaired)
  - Age*CR interaction

- The age*CR interaction term was the effect of primary interest in all models. It indicates a differential effect of age on CSF biomarkers as a function of CR (Low vs. High)
- All analyses were conducted using IBM SPSS, version 21.0. Only findings with p ≤ .05 (2-tailed) were considered to be significant

CONCLUSION

- High cognitive reserve is associated with reduced adverse age-related alterations in CSF biomarkers of AD
- Findings suggest a pathway through which cognitive reserve might favorably alter lifetime risk for symptomatic AD

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