Early Markers of Alzheimer Disease

https://www.neurodegenerationresearch.eu/survey/early-markers-of-alzheimer-disease/

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Research Abstract

The Baltimore Longitudinal Study of Aging (BLSA) was established in 1958 and is one the oldest prospective studies of aging in the USA and the world. The mission of the BLSA is to learn what happens to people as they get old and how to sort out changes due to aging from those due to disease or other causes. The Early Markers of Alzheimer’s Disease program continues to perform cognitive assessments and establish research diagnoses of Alzheimer’s Disease for BLSA participants. This information is used in multiple collaborative research projects conducted by intramural and extramural investigators, including our studies of brain

aging and neuroimaging biomarkers of cognitive decline and AD. Over the last year, we have continued cognitive assessments of BLSA participants, as well as diagnostic case conferences to establish research diagnoses of cognitive impairment. We have continued to investigate possible modifiers of cognitive aging, risk for dementia, and the presence of Alzheimer's pathology at autopsy. Highlights of our research program over the last year include a study of sex differences in cognitive trajectories over time. Although sex differences in the prevalence of Alzheimers disease are well-documented, sex differences in incidence are less clear. We hypothesized that if women were truly at greater risk for Alzheimers disease, they would show steeper cognitive declines during the asymptomatic preclinical period. We examined cognitive performance across a variety of measures in a large sample of 1065-2127 participants over a mean follow-up interval of 3.0-9.0 years and a mean of 2.3-4.4 assessments. Tests included measures of mental status, verbal learning and memory, figural memory, language, attention, perceptuo-motor speed and integration, executive function, and visuospatial ability. Analyses were limited to time points when participants were free of cognitive impairment. As expected, for both men and women, higher age at baseline was significantly associated with lower scores, and performance declined over time for all measures. After adjusting for age, education and race, sex differences in levels of performance were observed across most tests of specific cognitive abilities. At baseline, males outperformed females on the two tasks involving visuospatial ability, and females outperformed males in most other tests of cognition. Sex differences in trajectories of cognitive change over time indicated steeper rates of decline for men on measures of mental status, perceptuo-motor speed and integration, and visuospatial ability. In contrast, there were no measures on which women showed significantly steeper declines than men. These results highlight greater resilience to age-related cognitive decline in older women compared with men and suggest that the majority of the increased risk for AD in women is due to differential longevity. We also have continued to expand our collaborative efforts with Drs. Stephanie Studenski and Luigi Ferrucci and their postdoctoral fellow Teresa Tian to investigate the associations between age changes in cognitive and motor function and to investigate the neural underpinnings of these associations. In one study, we investigated whether higher intra-individual lap time variation of the 400-m walk predicts decline in executive function and whether the relationship is accounted for by slower walking. Using data on motor function and executive function from 347 BLSA participants aged 60 years and older, we found that higher lap time variation was associated with greater decline in performance on Trail-Making Part B and change in TMT B, independent of age, sex, education and mean lap time. These findings suggested that high lap time variation may be an early predictor of decline in executive function, independent of mean lap time. We also continue to collaborate closely with extramural investigators. In a study with Dr. Becca Levy of Yale University, we examined whether negative age stereotypes earlier in life predicted adverse brain outcomes decades later. We investigated this possibility in two samples from the BLSA -the autopsy subsample and the neuroimaging subsample. We examined whether negative age stereotypes predicted Alzheimers disease neuropathology at autopsy or hippocampal volume decline in the respective subsamples in dementia-free participants. Individuals holding more negative age stereotypes earlier in life had significantly steeper hippocampal-volume loss and significantly greater accumulation of neurofibrillary tangles and amyloid plaques, adjusting for relevant covariates. These findings suggest a new pathway to identifying mechanisms and potential interventions related to the pathology of Alzheimer's disease that merit further study.

Further information available at:

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