

Abstract

Background: The unequal distribution of social and health-related factors throughout the life course may lead to sex differences in dementia risk and cognitive aging. The aim of this thesis is to provide greater understanding of what drives the inequalities in cognitive aging between males and females. Specifically, we aimed to investigate sex differences in the rate of cognitive decline in European older adults (Study 1), in the association between childhood socioeconomic position and cognition (Study 2), number of children and risk of dementia (Study 3a), offspring sex and cognitive decline (Study 3b), and mild behavioral impairment and cognition (Study 4).

Methods: We performed five cohort studies using four cohorts of middle-aged and older adults residing in 21 countries across Europe, in Israel, and the United States. We sourced our data from the Survey of Health, Ageing and Retirement in Europe in Study 1 and Study 2, from the US Health and Retirement Study in Study 3a, from the US Adult Changes in Thought Study in Study 3b, and from the British Platform for Research Online to Investigate Genetics and Cognition in Aging in Study 4. Cognition was measured by tests on immediate recall, delayed recall and verbal fluency in Study 1 and Study 2, by immediate recall, delayed recall, serial 7s subtraction, and backwards counting tests in Study 3b, and by digit span, paired associate learning, self-ordered search, and verbal reasoning tests in Study 4. Dementia was diagnosed by a panel consensus based on DSM IV criteria in Study 3a. We used linear regression models, linear mixed-effects models, and Cox models in our analyses.

Results: In Study 1, the rate of cognitive decline in immediate recall (interaction sex \times time: $B=0.002$; 95% CI -0.001 to 0.006), delayed recall (interaction sex \times time: $B=0.000$; 95% CI -0.004 to 0.004), or verbal fluency (interaction sex \times time: $B=0.007$; 95% CI -0.005 to 0.020) was similar for males and females. However, when birth cohort and regional differences were considered, the rate of cognitive decline varied by sex. In Study 2, higher childhood socioeconomic position was associated with higher baseline cognition in both sexes, but to a larger extent in females ($B=0.238$; 95% CI 0.203 to 0.271) compared to males ($B=0.208$; 95% CI 0.180 to 0.235). Childhood socioeconomic disadvantage was associated with a higher rate of decline in delayed recall to a greater extent in females ($B=-0.023$; 95% CI -0.035 to -0.011) compared to males ($B=-0.018$; 95% CI -0.032 to -0.005). In Study 3a, fathers of four or more children had higher rates of dementia compared to fathers of two children (HR= 1.317 ; 95% CI 1.014 to 1.710), while we did not find any differences in rates of dementia in females. In Study 3b, we found a faster rate of cognitive decline in parents of at least one son ($B=-0.015$; 95% CI -0.029 to -0.002) compared to those without any sons, without any notable differences between sexes. In Study 4, mild behavioral impairment syndrome was associated with a lower level of paired associate learning score only in males ($B=-0.158$; 95% CI -0.245 to -0.072).

Discussion: Our findings suggest that there are nuanced variations in cognitive aging across different populations and birth cohorts, with potential differences between males and females. Our studies show that females and males are differentially impacted by early-life, midlife and later life risk factors. Future studies should not omit the importance of sex variations in the relationship between risk factors and cognitive aging.