A Life-Course Study of Cognitive Reserve in Dementia—From Childhood to Old Age

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Objective: *To test a life-course model of cognitive reserve in dementia and examine if school grades around age 10 years, formal educational attainment, and lifetime occupational complexity affect the risk of dementia in old age.* **Methods:** *7,574 men and women from the Uppsala Birth Cohort Multigenerational Study were followed for 21 years. Information on school performance, formal education, and occupational attainment was collected prospectively from elementary school archives and population censuses. Dementia diagnosis was extracted from the two Swedish registers. Discrete-time Cox proportional hazard models were estimated.* **Results:** *Dementia was diagnosed in 950 individuals (12.5%). Dementia risk was lower among individuals with higher childhood school grades (hazard ratio [HR]: 0.79; 95% confidence interval [CI]: 0.68 to 0.93) and was lower among individuals in data-complex occupations (HR: 0.77; 95% CI: 0.64 to 0.92). Professional/university education predicted lower risk of dementia in minimally adjusted models (HR: 0.74; 95% CI: 0.60 to 0.91), although the effect faded with adjustment for occupational complexity. Lowest risk was found in the group with both higher childhood school performance and high occupational complexity with data (HR: 0.61; 95% CI: 0.50 to 0.75). Importantly, high occupational complexity could not compensate for the effect of low childhood grades. In contrast, dementia risk was reduced in those with higher school grades, irrespective of occupational complexity.* **Conclusion:** *Higher childhood school performance is protective of dementia risk, particularly when preserved through complex work environments in adulthood, although it will remain protective even in the absence of later-life educational or occupational stimulation.* (Am J Geriatr Psychiatry 2015; ■:■−■)

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Dementia is one of the leading causes of disability, manifesting itself when the pathological processes in the brain reach the point of severe cognitive impairment.[1] Variations exist among individuals, however, in the degree of neuropathology required to cause the neuropsychological deterioration consistent with the clinical diagnosis of dementia.[2] To account for the discontinuity between the degree of brain damage and its clinical manifestation, the concept of *reserve* was proposed.[3] Biological attributes, such as brain size or synaptic connectivity, as well as aspects of life experiences, such as education or occupational characteristics, have been suggested as elements of reserve, protecting against the functional consequences of dementia neuropathology. Protection warranted by anatomical attributes has been referred to as *brain reserve*,[4] and compensatory mechanisms based on innate intelligence and life experience have been defined as *cognitive reserve*.[1,5]

Research on factors believed to influence cognitive reserve has consistently found an elevated risk of dementia in individuals with low education.[6,7] In addition to education, which is assumed to assist with brain network efficiency and flexibility,[8] it has been hypothesized that cognitive reserve may be influenced by occupational characteristics.[9] Demanding occupational roles that provide mental exercise and motivate individuals to continue to develop intellectual capacities have been found protective against dementia.[10,11] Education or occupational characteristics, however, can be affected by cognitive as well as social determinants.[12] Therefore, it can be argued that an early-life prerequisite for educational or occupational attainment, such as childhood cognitive ability, might be a more valid measure of reserve capacity,[13] although such measures are rarely available in dementia studies. The few that managed to obtain such information have reported elevated risk of dementia in individuals with low childhood cognitive ability.[14,15] It is, however, unclear to what extent education or occupational complexity continue to affect the risk of dementia when an early-life marker of reserve is taken into account, and a life-course model of cognitive reserve in dementia risk is yet to be tested.[16]

This is the first study to examine how dementia risk is affected by three factors influencing cognitive reserve, measured at different stages of the life-course: childhood, early adulthood, and mid-life. We can thereby analyze the relative importance of reserve components throughout the entire life-course in a large population-based study with prospectively collected exposure information, which has not been previously possible. We use school performance at age 10 years as a measure of early-life cognitive reserve, as previous research has indicated that the contribution of the cognitive component to teacher-assigned school grades is considerable.[17–19] Dementia diagnosis is extracted over a 21-year follow-up from two Swedish registers, which have previously been shown to be an appropriate source of dementia diagnoses.[20]

METHODS

Study Population

We conducted a cohort study of dementia risk using the Uppsala Birth Cohort Multigenerational Study.[21] This data set comprises 14,192 births registered at the Uppsala University Hospital between 1915 and 1929, and is broadly representative of the Swedish population during that historical period.[22] Of the 12,168 individuals alive and resident in Sweden in 1960 with register linkage, we excluded those who emigrated (N = 168), died (N = 1,792), or developed dementia before age 65 years (N = 26), leaving 10,182 eligible individuals. After exclusion of 2,608 participants with missing data, 7,574 individuals were followed for an average of 21 years (range of follow-up: 14–28 years).

Dementia Diagnosis

Dementia diagnosis was retrieved from the Swedish National Patient Register (NPR) as well as the Cause of Death Register (CDR).[23] During the period 1987–2000, the probability of detecting dementia in the NPR and the CDR combined has been 63% for prevalent cases and 39% for incident cases, and specificity was 98%.[20] Because of improved diagnostics, increased awareness of the disease, and growing register validity over time,[24] recording in the public records can be assumed to have changed between 1980 (start of the follow-up for the oldest individuals) and 2008 (end of the follow-up). To take