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Invited Commentary | Geriatrics

Intelligence, Cognitive Reserve, and Dementia Time for Intervention?

Tom C. Russ, PhD, MRCPsych

Alzheimer dementia is now recognized to be a disease of the whole life course and it is accepted that, while the neuropathological changes of Alzheimer disease develop decades before the clinical symptoms of dementia begin, important risk factors can have their effect much earlier in life, perhaps even before birth.¹

Huang and colleagues² report findings from a large cohort study of male and female high school students who completed a variety of cognitive tests and who were passively followed up later in life to identify who had developed Alzheimer dementia. The authors found that better cognition measured during high school was associated with decreased odds of dementia later in life. For the first time they were able to disentangle different cognitive skills and found that mechanical reasoning and memory for words were particularly important.

Two well-known studies in this area are the Nun Study and the Lothian Birth Cohort (LBC) studies of 1921 and 1936.^{3,4} The Nun Study analyzed autobiographies completed as novices entering the convents for idea density and grammatical complexity and found that low linguistic ability in early life was associated with poorer cognitive function later in life and more Alzheimer disease pathology.

The LBC (and parallel Aberdeen Birth Cohort [ABC]⁵) studies followed up samples of 2 comprehensive national intelligence tests of 11-year-old schoolchildren in Scotland in 1932 and 1947.^{6,7} Both the LBC 1921 (550 participants at baseline) and the LBC 1936 (1091 participants at baseline) have been followed up at multiple waves since recruitment in later life and this process is continuing for the younger cohort.⁸ The ABC 1921 study investigators reported back in 2000 that lower childhood mental ability (based on performance on the Moray House Test) was associated with an increased risk of dementia.⁹ A later case-control study using the LBC 1921 study suggested that there might be a differential effect with different dementia subtypes—intelligence might be more related to vascular dementia than Alzheimer dementia.⁵

More recently, we linked the whole Scottish Mental Survey 1932 cohort (32 467 participants traced)—in contrast to the samples who have been followed up face-to-face in the LBC/ABC studies—to electronic health records and death certificates and explored the association between childhood mental health ability and dementia occurrence. The pattern of association differed between the sexes in that there was a dose-response association between lower intelligence and dementia risk in women but not in men, although risk was increased in the lowest intelligence groups in both sexes.

The hypothesis behind all these studies of cognitive reserve or brain reserve is that some people's brains may be more resilient to aging and neurodegeneration than others'. The study by Huang and colleagues² furthers our understanding in this area and there are now multiple high-quality epidemiological studies linking poorer intelligence in early life with dementia risk. However, as with all observational research, there remains the need to clarify whether these associations are causal. Further complicating interpretation of these studies is the fact that intelligence is a complex trait, is subject to genetic influences, and potentially has a bidirectional relationship with socioeconomic status and education.¹⁰

However, given that we have a plausible mechanism—cognitive reserve—we now need to consider interventional research. The International Federation on Aging Copenhagen Summit on cognitive reserve in 2017 highlighted a number of factors that could potentially influence cognitive

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reserve, including modifiable health factors, education, social support, positive affect, stimulating activities and/or novel experiences, and cognitive training (<http://www.ifa-copenhagen-summit.com/>). Not all of these are modifiable, and of those that are, not all are modifiable later in life, but the potential of intervening at many different stages of the life course to improve one—or ideally multiple—of these factors is there. If, as a result, cognitive reserve could be modified before the clinical onset of dementia (even if Alzheimer disease were present in the brain), this may delay the onset of these clinical symptoms which would, in turn, reduce the number of people affected by dementia worldwide. Given the growing global public health burden of dementia, this is a vital question.

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Corresponding Author: Tom C. Russ, PhD, MRCPsych, Alzheimer Scotland Dementia Research Centre, University of Edinburgh, 7 George Sq, Edinburgh EH8 9JZ, United Kingdom (t.c.russ@ed.ac.uk).

Author Affiliations: Alzheimer Scotland Dementia Research Centre, University of Edinburgh, Edinburgh, United Kingdom; Centre for Cognitive Ageing and Cognitive Epidemiology, University of Edinburgh, Edinburgh, United Kingdom; Centre for Dementia Prevention, University of Edinburgh, Edinburgh, United Kingdom; NHS Lothian, Edinburgh, United Kingdom.

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