Cognitively stimulating activities to keep dementia at bay

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Dementia affects a staggering proportion of individuals, imposing a huge cost to our society. There are currently no disease-modifying treatments for dementia, making lifestyle factors that influence dementia risk of utmost importance. One such lifestyle factor that has shown promise in delaying dementia onset is engagement in cognitively stimulating activities, such as reading, writing, and playing games.[1,2] However, the mechanisms by which these activities exert protective effects remain unclear (figure).

In the current issue of *Neurology*®, Wilson et al.[3] investigated whether childhood (6–12 years), young adulthood (age 18), middle age (age 40), and current engagement in cognitively stimulating activities slows cognitive decline. Given the availability of neuropathologic assessments on 294 individuals followed clinically every year on average 5.8 years before death, they were able to test the "cognitive reserve hypothesis" vs the "reverse causality hypothesis." Specifically, does engagement in cognitive activities delay or slow cognitive decline (construct of cognitive reserve[4]) or is cognitive inactivity caused by underlying pathology (reverse causality)? Arrows 1–3 in the figure show the reserve mechanisms through which cognitively stimulating activities may slow cognitive decline: 1 suggests an independent effect on cognition; 2 suggests that it lowers accumulation of pathology; and 3 suggests an interaction of cognitively stimulating activities with pathology. By contrast, arrow 4 illustrates reverse causality. A key strength of this study is the availability of the neuropathologic measures of amyloid burden, tangle density, gross cerebral infarcts, microscopic cerebral infarcts, and neocortical Lewy bodies that allowed the authors to test the 2 hypotheses. Wilson et al. found that lifetime (early and late) engagement in cognitively stimulating activities slows cognitive decline, accounting for 14% of the residual variability in cognitive decline that is independent and beyond what is explained by neuropathology. Interestingly, both more frequent current and early-life engagement in cognitively stimulating activities were shown to independently slow late-life cognitive decline.

Overall, the results support the cognitive reserve hypothesis by suggesting that individuals with high lifespan levels of cognitive activity show slower decline despite the presence of underlying pathology. Consistent with in vivo work, this finding suggests that the mechanism by which reserve exerts a protective effect is not directly through reduction of pathology[5,6] (however, see reference 7). If reserve does not exert an effect through pathology, a major question remains as to how cognitive activity offers protection against decline. As suggested by others, it is also possible that in individuals with high cognitive reserve and pathology, an association between measures of pathology and cognitive reserve may help preserve cognition[8,9] (figure). Another exciting finding in the article by Wilson et al. is that current cognitive activity slowed the rate of cognitive decline years before death. This finding potentially addresses a question that all of us ask from time to time—can we do anything to slow down late-life cognitive decline? The results suggest yes—read more books, write more, and do activities that keep your brain busy irrespective of your age.

While we have come a long way in improving our understanding of mechanisms through which cognitively stimulating activities are protective against dementia, we need larger cohorts, longer follow-ups, serial biomarker measurements antemortem, and neuropathologic details postmortem to understand these relationships. We also need to investigate the effect of cognitive reserve on measures of neural structure and function as well as cognition in the absence of pathology, i.e., younger or older individuals lacking evidence of underlying pathology. Developing sensitive in vivo biomarker measures, as well as neuropsychological tests that provide detectable decline in cognition irrespective of an individual's level of cognitive reserve, is necessary (which may be especially relevant to detect treatment effects among clinically normal individuals participating in secondary prevention trials[10]). Our field will also benefit from establishing better proxies to capture the construct of cognitive reserve, which often vary across laboratories, making direct comparison of results problematic. The

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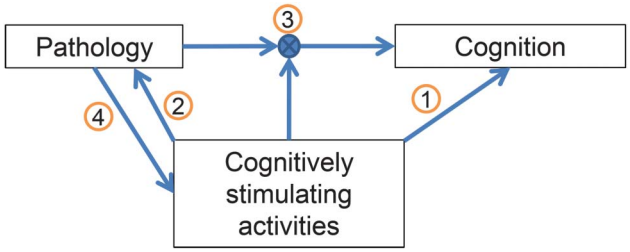
Figure **Models that explain the effect of cognitively stimulating activities on the relationship between pathology and cognition**



References 3, 5, and 6 support the existence of arrow 1 that is independent of neuropathology, reference 7 supports the existence of arrow 2, and references 8 and 9 support the interaction between cognitive reserve and pathology (arrow 3). References 6, 8, and 9 did not measure engagement of cognitive activities directly, instead using verbal IQ and education as proxies of cognitive reserve.

ongoing research in the field will soon be able to educate neurologists on the cognitive outcomes that can be expected in a patient with high cognitive reserve vs low cognitive reserve and the steps that may alter the course of disease. Until then, the best advice is simple: "a busy mind to keep dementia at bay."

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