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COMMENTARY

Can reading increase cognitive reserve?

In this issue of *International Psychogeriatrics*, Chang *et al.* (2020) present findings from a secondary analysis of the Taiwan Longitudinal Study on Aging, a longitudinal study started in 1989. Their analyses included 2946 individuals without severe cognitive impairment, of which 818 had 14 years of follow-up. The authors investigated the effects of reading activity and education on cognitive decline, as defined by an increase of two or more points in a modified version of the Short Portable Mental Status Questionnaire. The authors found that high reading activity, as defined by almost daily reading, was associated with lower odds of cognitive decline, compared to low reading activity. This finding remained relatively consistent both in individuals with and without mild cognitive deficits at baseline. Higher education was also separately associated with lower odds of cognitive decline. While findings on the effects of reading based on education level were mixed in the 6-year and 10-year follow-up periods, protective effects of higher reading frequency were observed across all education levels at 14-year follow-up, including the low-education group, which consisted of individuals who were illiterate or literate without formal education.

These findings extend previous research on the effects of cognitive reserve on the risk of progression to mild cognitive impairment (MCI) and dementia. The construct of cognitive reserve was derived from observations of discrepancies between the presence of dementia-related neuropathology and cognitive or functional impairments in individuals (Negash *et al.*, 2013). Although there are some differences across studies on how "cognitive reserve" is measured, it has been defined in a whitepaper published by members of the Reserve, Resilience, and Protective Factors Professional Interest Area as "the adaptability of cognitive processes that helps to explain differential susceptibility of cognitive abilities or day-to-day function to brain aging, pathology, or insult" (Stern *et al.*, 2018).

As a theoretical construct, cognitive reserve cannot be measured directly. Instead, it is most frequently measured using proxies assumed to contribute to the development of cognitive decline, including education, occupational complexity, and leisure activities – protective factors that have been identified primarily through epidemiological research. The most commonly used proxy for cognitive reserve is education history (Pettigrew and Soldan, 2019). Most, but not all, studies have found that lower education is associated with greater incidence and prevalence of dementia (Sharp and Gatz, 2011; Valenzuela and Sachdev, 2006), as well as age-related cognitive decline (Lenehan *et al.*, 2015). Higher education has been associated with a reduction in dementia risk in a linear dose–response manner (Xu *et al.*, 2016), and its effect has been noted in some, but not all, reviews to be stronger in studies that have included individuals with no or low education (Sharp and Gatz, 2011).

Findings from longitudinal studies on the trajectory of cognitive decline have been mixed. Some studies have found no association between education and rate of cognitive decline in individuals without dementia at baseline, while others have reported slower or faster decline (Lenehan *et al.*, 2015). Inconsistencies in the prior literature on the relationship between education as a proxy measure for cognitive reserve and longitudinal trajectory of cognitive outcomes have been attributed, among a number of factors, to differences in methodology and accounting for MCI and baseline (Lenehan *et al.*, 2015).

Other proxies for cognitive reserve, such as occupational attainment, premorbid intelligence, and participation in mentally stimulating leisure activities, have also been associated with decreased risk of developing dementia (Valenzuela and Sachdev, 2006). Leisure activities, such as knitting, walking, taking classes, physical conditioning, doing volunteer work, and participation in social activities, have been associated with lower risk of developing Alzheimer's disease (AD) in older adults (Valenzuela and Sachdev, 2006). Being engaged in a variety of activities may be more important than frequency of activities in reducing the risk of cognitive decline (Carlson *et al.*, 2012). In particular, participation in activities that are mentally stimulating appears to have a more robust effect than social and physical activities on the risk of cognitive decline and dementia (Yates *et al.*, 2016). Randomized controlled trials of cognitive training interventions, most of which have follow-up periods limited to 1 year or less, have reported improvements in measures of instrumental activities of daily living for individuals with normal

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cognition at baseline, and improvements in performance on cognitive tests in participants with normal cognition and MCI (Fan and Wong, 2019).

Although higher cognitive reserve is associated with lower incidence and time to cognitive symptom onset, studies that have accounted for cognitive trajectories before and after diagnosis of MCI/dementia have reported accelerated decline after the symptom onset of MCI and dementia, suggesting that the mechanism by which cognitive reserve is protective for cognitive function is by delaying the onset of symptoms rather than reducing the rate of cognitive decline (van Loenhoud *et al.*, 2019). Similar to patterns observed between higher education and trajectory of cognitive decline, more rapid decline in cognitive function has been observed in individuals with dementia who engaged in more leisure activities (especially intellectual activities) prior to dementia onset (Helzner *et al.*, 2007).

A proposed explanation for these observations is that individuals with higher cognitive reserve do not experience cognitive decline until pathology is at a more advanced stage. Thus, by the time they begin experiencing cognitive symptoms, pathology quickly overwhelms the ability to maintain function through alternative, compensatory pathways (Stern, 2012). There is some evidence that protective effects of cognitive reserve on cognitive decline decreases as markers of neuronal injury, such as cortical atrophy (Mungas *et al.*, 2018), and markers of AD pathology (Soldan *et al.*, 2013) increase. A recent study found that the effect of brain atrophy is greater in individuals with a greater rate of depletion in cognitive reserve (estimated by deviation of cognitive function from expected trajectory based on baseline demographics and neuroimaging measurements) (Bettcher *et al.*, 2019). These findings suggest that the effect of brain pathology on cognitive decline may increase as the compensatory processes of cognitive reserve decrease with disease progression.

While epidemiological studies have demonstrated that aspects of life experience can build cognitive reserve against age- or disease-related dementia pathology, the precise components needed to improve cognitive reserve remain unclear (Stern, 2012). Further complicating its study is the dynamic nature of cognitive reserve, meaning that it can be influenced by different experiences across a lifespan. While knowledge of the relationship between cognitive reserve proxies and pathological brain markers may improve understanding of the dynamic nature of cognitive reserve, epidemiologic research on cognitive reserve has generally been limited by a lack of measures of underlying pathology. Although studies that have included biomarker measures of cognitive reserve have generally demonstrated that cognitive reserve modulates the relationship between neuropathology and cognitive status, these studies have mostly been cross-sectional, limiting the ability to make inferences about causation (Pettigrew and Soldan, 2019). Longitudinally, there is some evidence that higher education may have protective effects from the impact of white matter lesions and cortical thinning on the risk of progression to dementia, though evidence that proxies of cognitive reserve outside of physical activity can attenuate the development of brain pathology is limited (Pettigrew and Soldan, 2019).

Study on whether cognitive activities moderate the relationship between dementia pathology and cognitive decline is limited, and findings have been mixed. In a longitudinal study of individuals with subjective cognitive decline and MCI, cerebrospinal fluid (CSF) Aβ42, CSF tau, and hippocampal volumes were not associated with lifestyle factors in later life, including social, physical, and cognitive activities (Reijs *et al.*, 2017). While those biomarkers were associated with conversion to dementia, they did not find evidence that this relationship was modulated by lifestyle factors. In contrast, recent analyses of the Rush Memory and Aging Project cohort consisting of individuals with intact cognition and MCI at baseline reported that high lifespan cognitive reserve (consisting of education, early-life, midlife and late-life cognitive activities, and social activities in late-life) was associated with decreased risk of progression from normal cognition to MCI, and from MCI to dementia (Xu *et al.*, 2020). When brain pathology was considered, lifespan cognitive reserve remained associated with lower risk of progression from MCI to dementia even in individuals with high levels of AD pathology or infarcts on autopsy.

Chang *et al.*'s findings are consistent with prior studies that have found that higher education and cognitively stimulating activities are associated with lower risk of cognitive decline. Like any study, there are limitations which the authors have discussed at length, including reliance on self-report and utilization of reading measures from one time point. It should be noted that the cohort consisted of a wide range of reading and education levels. Due to limitations in sample size, the moderate reading frequency groups in this study were analyzed as "low" reading frequency. Thus, the comparison between "high" and "low" reading frequencies was primarily amongst individuals who "never" read and individuals who read "almost every day." While there may be limitations in extrapolating to other groups not on the extremes of the activity and education spectrum, it nevertheless provides valuable insights into the effects of reading across different education levels.

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Although 28.5–39% of the cohort was reported to be illiterate, Chang *et al*. found that reading activity may be beneficial across a range of educational backgrounds. Despite the pattern of findings being mixed at different time points, it provides grounds to consider education level-dependent effects of cognitively stimulating activities in future studies. Studies on the effects of reading on the long-term rate of cognitive decline (Sörman *et al*., 2018), the difficulty level of reading materials required for effect, and whether continued reading is required to maintain protective effects on cognition are limited. Given that education is primarily achieved early in life, further understanding of the impact of cognitive reserve factors modifiable in later stages of life is needed. Future studies examining the effect of reading in the context of biomarkers, across different time points, may provide further insight into its relationship with other proxies of cognitive reserve and cognitive decline.

Conflict of interest

None.

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