Educational attainment and cognitive status in MS: Reading, writing, and economics

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Cognitive impairment is a prevalent and debilitating consequence of multiple sclerosis (MS; for review, Rocca et al.1) for which we have no effective treatments.2 The best approach to ‘treatment’ may be early intervention to prevent cognitive decline; however, a science and clinical practice of early intervention/preventative medicine requires accurate identification of patients at greatest risk of future cognitive decline, which is currently quite difficult. Research presented within this issue may advance early identification of at-risk MS patients. Silva and colleagues3 identify lower educational attainment as a risk factor for cognitive impairment in 419 Portuguese MS patients: cognitive impairment was more common among patients with lower (≤ 9 years, 25% of patients impaired) versus higher (> 9 years, 15% of patients impaired) educational attainment. Findings were most pronounced for cognitive efficiency and memory: the cognitive domains most affected by MS.1 By comparison, only 3% of 159 healthy controls were cognitively impaired.

These results are consistent with a growing literature on cognitive reserve in MS (for review, Sumowski and Leavitt4), which shows that MS patients with higher educational attainment (e.g. Benedict et al.5), intelligence (e.g. Sumowski et al.6), and mentally-stimulating lifestyles (reading, writing, hobbies, e.g. Sumowski et al.7) are at lower risk for cognitive decline/impairment. Silva and colleagues advance this literature by investigating reserve in a large cross-sectional sample representing about 80% of patients seen at an outpatient MS clinic. This may be the largest MS sample used in reserve research to date, which affords more confident generalization to the MS population. Also, use of educational attainment as a proxy of reserve has utility, as this demographic information is readily available to clinicians.

On the one hand, it may not seem surprising that educational attainment predicts cognitive status. Importantly, however, Silva and colleagues adjusted cognitive performance for education before examining the link between educational attainment and risk for cognitive impairment. As such, the reported link between higher education and lower risk for cognitive impairment cannot be simply explained by higher premorbid cognitive function. Instead, patients with higher education performed closer to education-adjusted expectations, whereas patients with lower education performed worse than expected, which is consistent with the reserve hypothesis.

Educational attainment is not normally distributed, but, rather, has a bimodal or multimodal distribution. The authors dichotomized educational attainment based on expectations within the Portuguese educational system (≤ 9 years versus > 9 years), which provides a useful cutoff in Portugal and a proof of concept for other countries, where the most informative educational cutoff will differ based on their respective systems. For instance, based on United States Census Bureau data on highest level of education achieved (www.census.gov/hhes/socdemo/education), there is at least a trimodal distribution: high school diploma (12 years, 29.7%), some college or associates degree (13 to 15 years, 21.0%), bachelor’s degree or higher (≥ 16 years, 32.0%). Even within the United States normative expectations for educational attainment differ widely by state (e.g. 20% in Mississippi to 40% in Massachusetts), which may be important to consider.

Despite the ease and availability of educational attainment as a predictor of cognitive impairment, it is difficult to isolate the exact mechanism by which higher education is protective. Consistent with the cognitive reserve hypothesis, educational attainment may be a proxy for intelligence or intellectual enrichment (e.g. literacy). Importantly, educational attainment also is a proxy of socioeconomic status (SES), which likely contributes to lifestyle and health-related outcomes. Indeed, epidemiologic research has linked lower education (as a proxy of SES) to increased prevalence of chronic diseases, including neurologic diseases, among Europeans.8 Moreover,
lower SES (using education as a proxy) has been linked to higher levels of circulating inflammatory factors (e.g. tumor necrosis factor-α, interleukin-6) in European\(^9\) and American\(^10\) cohorts, as well as unhealthy lifestyles (e.g. physical inactivity, obesity).\(^9\) As such, in addition to explanations related to intellectual enrichment and cognitive reserve (for review, Sumowski and Leavitt\(^4\)), aforementioned links among education, SES, lifestyle, and health may further explain worse cognitive outcomes among MS patients with lower educational attainment reported by Silva and colleagues. This does not diminish the potential utility of educational attainment as a marker of risk for cognitive impairment, but instead encourages future research to examine the specific mechanisms of action responsible for the link between lower education and higher risk for cognitive impairment.

As discussed, clinical consideration of proxies for cognitive reserve (e.g. education, intelligence) may improve our ability to identify MS patients at greatest risk for cognitive impairment, which is a prerequisite for a science and clinical practice of early intervention/preventative medicine. The current research by Silva and colleagues makes an important contribution toward this end, especially because their study was conducted in a large representative sample of MS patients. Importantly, however, predictors such as educational attainment and intelligence are fixed, stable proxies of reserve, and are therefore not viable targets for intervention. We have observed that engagement in cognitive leisure activities (e.g. reading, writing, hobbies) during adulthood contributes to reserve against cognitive impairment in MS patients independently of educational attainment and intracranial volume (an estimate of genetically-mediated brain reserve).\(^7\) Such observational work engenders hope that lifestyle factors within a patient’s control may be protective, and can therefore be a target for early intervention. The next step is to move beyond observational designs toward experiments (clinical trials) aiming to build reserve in MS patients, which will provide the strongest evidence for, and clinical utility of, the reserve hypothesis.

### References