EDITORIAL

Does cognitive reserve apply to multiple sclerosis?

Peter A. Arnett, PhD

Address correspondence and reprint requests to Dr. Peter Arnett, Penn State University, Psychology Department, 522 Bruce V. Moore Bldg., University Park, PA 16802-3105 paa6@psu.edu

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Cognitive reserve (CR) is the degree of spare cognitive capacity available to protect against the effects of disease or trauma to the brain.[1] Individuals with more CR are theorized to be less likely to show cognitive changes associated with neurologic change. CR has mostly been studied in Alzheimer disease (AD); there is significant support for CR buffering the effects of AD. A seminal study found significant postmortem evidence for AD pathology in the brains of 10 elderly individuals whose brains were larger than average and who had not shown any clinical signs of AD while living.[2]

In this issue of *Neurology*®, Sumowski and colleagues[3] studied CR in patients with multiple sclerosis (MS), making a central contribution. The authors tested 44 patients with MS using a task of memory and learning known as the Selective Reminding Test. The authors chose to examine memory, because memory deficits are often the most commonly reported cognitive problems in MS.[4] Importantly, although neuroimaging indices (e.g., brain atrophy) can partially explain lower performance on such tasks, such indices can only account for about 10%–15% of variance. The authors reason that CR may partially explain this limited effect. To examine this, the authors asked whether performance on the memory and learning task was predicted by brain atrophy (third ventricle width), a CR measure, and the interaction of these factors. Results supported the CR hypothesis, with the interaction explaining 7% of unique variance in immediate recall and 9% in delayed recall after accounting for the direct influence of brain atrophy and CR. Thus, the study supported the notion that CR buffers the effects of brain atrophy on learning and memory performance in MS. The study also complements findings from the authors' recent study examining CR in the context of cognitive efficiency.[5]

By demonstrating that the construct of CR is applicable to patients with MS, these investigators have opened up a whole new domain of inquiry in MS with important clinical applications. Recent research in AD has identified several interventions linked to improved CR, including increased physical activity, social interaction, and challenging mental activities.[6,7] CR thus represents a potentially modifiable variable that could reduce or prevent cognitive problems in MS. This possibility is particularly appealing as patients with MS typically live many years following their diagnosis,[4] and also because currently available cognitive interventions have had minimal success in MS. Enhancing CR could thus be implemented at an early stage of the disease, when the impact of the disease on the brain is typically less and when such interventions would likely be most effective.

Though provocative, the study has important limitations. First, the authors' method for accessing CR through a measure of intellectual enrichment is limited. Using the Wechsler Vocabulary subtest, the authors note that vocabulary skills are correlated with educational attainment and frequent reading. However, the use of additional CR indices would have provided a richer and more complete estimation of this construct. In the AD literature where the CR construct has been more developed, investigators have often supplemented measures of vocabulary with indices of education and occupation,[1] as well as procedures that assess lifetime involvement in leisure and cognitively stimulating activities, and involvement in physical and social activities.[8] Second, the authors' assessment of learning and memory is limited, measured using only 1 task. A more broad-based assessment of learning and memory would help to establish the finding as being relevant to learning and memory more generally, as opposed to task-specific. A third limitation, acknowledged by the authors, is that the average educational level of the sample was about 16 years, so the results may not generalize to the overall MS population. The authors speculate that such effects might be more pronounced among lower functioning patients; this is a reasonable speculation, requiring an additional study to address. A final limitation that also relates to the

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From the Department of Psychology, Penn State University, University Park, PA.
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generalizability of the results concerns the patients' performance on the learning and memory task. It is unclear whether the overall patient group was impaired on this task, as the raw or standardized data are not presented. If the patients were not impaired on the task, then this would limit the generalizability of the findings, because the patients would not be representative of the typically memory-impaired MS sample. A future study that attempts to address these limitations would strengthen the authors' hypothesis that CR can provide a buffer against learning and memory problems in MS.

The research on CR in MS is too new, and the authors' sample too small, to justify the formulation of firm clinical guidelines. However, the data suggest that it would be reasonable to encourage patients with MS to engage in activities that might enhance CR. For example, encouraging patients to engage in regular exercise, actively pursue social relationships, and engage in mentally stimulating activities might maintain or improve CR and help to buffer patients against the long-term cognitive effects of the disease.

Limitations aside, Sumowski and colleagues' study[3] raises the important question: "Does cognitive reserve apply to multiple sclerosis?" The provisional answer is "yes." The study applies an important theoretical construct that has been well-developed in the AD literature to MS and suggests numerous avenues for future work that could have significant implications for preventing or treating cognitive problems in MS.

DISCLOSURE

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