EDITORIAL

Promoting physical activity to control multiple sclerosis from childhood

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Neurology® 2015;85:1644–1645

Multiple sclerosis (MS) is a costly disease for society, because it affects young people and has a relentless course with progressive accumulation of physical disability and cognitive deficits. MS is expensive not only because of the high prices of available treatments,[1] but also because of reduced employment/job retention for patients and their caregivers. This is especially true for patients with disease onset during childhood, who usually reach more severe disability at a younger age than those with adult-onset MS.

The identification of factors that could reduce the burden of disease, in addition to pharmacologic treatment response, is of paramount importance, because it might improve our understanding of the mechanisms responsible for MS clinical manifestations and also may provide novel targets for therapeutic interventions. Part of this effort is defining whether specific lifestyle attitudes and habits may influence the disease.

An interesting recent observation is the demonstration of the potential role of cognitive reserve in explaining the incomplete relationship between brain structural damage (quantified in terms of T2 lesions or atrophy) and cognitive status in patients with MS.[2] The reserve theory posits that environmental factors derived from life experience, quantified in terms of intellectual enrichment, educational attainment, vocabulary, and occupational activities, contribute to reserve against disease-related cognitive impairment. Longitudinal observations in adult patients with MS have also suggested that higher intellectual enrichment may protect from incipient cognitive decline.[3]

Physical activity is another modifiable variable deserving proper investigation; it contributes to cognitive reserve, and the capacity for physical activity in youth is less likely influenced by age differences than is intellectual experience. In their study published in this issue of *Neurology*®, Grover et al.[4] explored the association among physical activity, relapse rate, depression, and fatigue in a cohort of children with MS (n = 31) and monophasic acquired demyelinating syndrome (mono-ADS) (n = 79) attending a specialized pediatric MS clinic. The first interesting finding of this study is that, compared with mono-ADS, pediatric patients with MS reported less strenuous and total physical activity, with a lower proportion of these patients participating in strenuous physical activity. Such a finding was not due to between-group differences in severity of clinical disability, sex, or age, as evidenced by group subanalyses. Moreover, patients with MS practicing less physical activity had higher levels of fatigue and depression than those practicing more physical activity. The cross-sectional study design does not allow determination of causality: Does less physical activity worsen fatigue and depression? Or are fatigue and depression among the reasons for reduced physical activity? However, these findings agree with those from adults with MS.[4] Although not proven by the current investigation, several pieces of evidence suggest that regular physical exercise not only improves aerobic capacity, cognitive performance, and muscular strength, but also reduces fatigue and depression. This is independent of disease entity, having been reported in elderly healthy individuals as well as in adults and children with neurologic, psychiatric, and chronic conditions.[5–7]

What are the mechanisms explaining the generalized effect of physical exercise? Studies on healthy and diseased adults focusing on aerobic training described an effect on structural MRI measures of white matter architecture integrity as well as increased volume of specific gray matter structures, including the hippocampus.[8,9] Healthy adolescents with greater fitness levels have larger volumes of deep gray matter.[10] Although the neurobiological substrates underlying such brain structural changes are largely unknown, exercise-induced increases in hippocampal cerebral blood flow, measured with MRI, correlated with postmortem measurements of neurogenesis.[11] Physical activity may lessen chronic low-grade inflammation in children with chronic inflammatory conditions.[12]

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Go to Neurology.org for full disclosures. Funding information and disclosures deemed relevant by the authors, if any, are provided at the end of the editorial.

Clearly, whether these findings can be translated into ad hoc strategies of physical training of pediatric populations needs to be investigated. The beneficial effects of physical activity might be influenced by the level of maturation of the CNS in the pediatric population: on the one hand, the incomplete development of the CNS might result in increased susceptibility to disease-related damage; on the other—especially in very young children—incomplete myelination and the potential for plasticity could lessen vulnerability to such damage.

The second intriguing finding of the study by Grover et al. comes from the analysis of MRI measures of disease burden (brain T2 lesions and atrophy), obtained from a subsample of patients, which revealed that patients with strenuous physical activity also had lower T2 lesion volume and lower annualized relapse rate than the others. Explaining why patients with MS who practice strenuous physical activity should have fewer brain T2 lesions is challenging. An influence of disability is unlikely, since the degree of disability in these patients was relatively low. In addition, in adult patients with relapsing-remitting MS, higher physical activity has been correlated with lower disability, better quality of life measures, and reduced relapse rate.[13] Whether these results might be related to a better way of perceiving or living with a stressful disease is a hypothesis that needs to be considered. Indeed, stressful conditions are associated with relapses and MRI activity in patients with MS.

The current study offers tantalizing results that have the potential to guide future studies, which ideally would be longitudinal, to allow some statements about causality. Still, many unanswered questions would remain, concerning not only the type, duration, and frequency of ideal physical activity, but also factors influencing performance, whether cognitive or physical (e.g., anxiety). What should be the timing of physical activity with respect to age at disease onset or to level of clinical impairment? A strong message from this study is that implementing physical activity may represent an easy approach that could favorably influence disease outcome in the long term.

STUDY FUNDING

No targeted funding reported.

DISCLOSURE

M.A. Rocca received speaker honoraria from Biogen Idec, Novartis, and ExceMed and receives research support from the Italian Ministry of Health and Fondazione Italiana Sclerosi Multipla. M. Filippi serves on scientific advisory boards for Teva Pharmaceutical Industries; has received compensation for consulting services and/or speaking activities from Biogen Idec, Bayer, ExceMed, Merck Serono, Novartis, Sanofi, and Teva Pharmaceutical Industries; and receives research support from Biogen Idec, Teva Pharmaceutical Industries, Novartis, Italian Ministry of Health, Fondazione Italiana Sclerosi Multipla, Cure PSP, Alzheimer's Drug Discovery Foundation (ADDF), the Jacques and Gloria Gossweiler Foundation (Switzerland), and ARiSLA (Fondazione Italiana di Ricerca per la SLA). K. Deiva received funds as national PI for studies from Merck Serono, Novartis, and Sanofi, and travel subsidies and speaker fees from Biogen Idec. Go to Neurology.org for full disclosures.

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