

OPEN

Rehabilitation in multiple sclerosis

Commentary on the recent AAN systematic review

Matthew H. Sutliff, PT, MSCS; Susan E. Bennett, PT, DPT, EdD, NCS, MSCS; Patricia Bobryk, MHS, PT, MSCS, ATP; June Halper, MSN, APN-C, MSCN; Lori A. Saslow, MS; Lisa T. Skutnik, PT, MA, MA; Christine Smith, OTR/L, MSCS; Kathleen Zackowski, PhD, OTR, MSCS, CRND; David E. Jones, MD

Multiple sclerosis (MS) is one of the most common causes of nontraumatic neurologic disability in young adults in the United States. Historically, MS care focused on rehabilitation and symptomatic management; however, this focus broadened with the development of disease-modifying therapies (DMTs), resulting in pharmacologic treatments that effectively reduce relapses and potentially slow the progression of disability. Consequently, DMTs often dominate many discussions regarding MS care, regardless of the fact that they do not reverse disability or restore function, arguably the primary goal of those with MS. Comprehensive, multidisciplinary care goes beyond the management of DMTs in MS treatment plans and strives to improve patient outcomes, functionality, and quality of life, goals that will likely prove to hold considerable importance as health care reimbursement transitions from a fee-for-service to a value-based paradigm. It is therefore likely that achieving improvement in some of the outcomes delineated in the American Academy of Neurology's (AAN) quality measures for MS will necessitate involvement of rehabilitation specialists.¹

The Guideline Development, Dissemination, and Implementation Subcommittee of the AAN recently published "Summary of Comprehensive Systematic Review: Rehabilitation in Multiple Sclerosis."² The objective of this systematic review was to examine, within an evidence-based practice (EBP) framework, research studies investigating rehabilitation treatments in MS and clearly states that their analysis was limited by a lack of well-designed studies of rehabilitation in MS. This review found that there is moderate evidence supporting the efficacy of 8 weeks of weekly physical therapy for improving disability in the context of balance and gait but not upper extremity function. Beyond that, it found weaker evidence for several other rehabilitative interventions in MS, suggesting that comprehensive cross-specialty rehabilitation, individualized exercise programs, motor balance training, breathing-enhanced arm exercises, and inspiratory muscle training possibly are effective but require further study.²

It is notable that most of the interventions addressed in this systematic review involved physical therapy and seemingly omitted several disciplines of importance to people with MS. This may suggest that the data supporting physical therapy data are more robust. However, it may also suggest that because rehabilitation professionals from physical therapy, occupational

Mellen Center for MS Treatment and Research (MHS), Neurological Institute, Cleveland Clinic, OH; University of Buffalo (SEB), SUNY, NY; Comprehensive Care Center of Central Florida (PB), Orlando; Consortium of Multiple Sclerosis Centers (JH, LTS), International Organization of MS Nurses, Hackensack, NJ; LS Science & Medical Communications, LLC (LAS), Great Neck, NY; Center for Physical Rehabilitation (CS), Holy Name Medical Center, Teaneck, NJ; Kennedy Krieger Institute (KZ), Johns Hopkins University School of Medicine, Baltimore, MD; and University of Virginia Health System (DEJ), Charlottesville.

Funding information and disclosures are provided at the end of the article. Full disclosure form information provided by the authors is available with the **full text of this article at Neurology.org/cp**. The Article Processing Charge was paid by the Consortium of Multiple Sclerosis Centers.

This is an open access article distributed under the terms of the Creative Commons Attribution-NonCommercial-NoDerivatives License 4.0 (CC BY-NC-ND), which permits downloading and sharing the work provided it is properly cited. The work cannot be changed in any way or used commercially.

Correspondence to: Dj9d@virginia.edu

Supplemental Data

Neurology.org/cp

therapy, speech language pathology, and exercise physiology were not represented on the review panel, their input was not included in the systematic review. Two examples in which the inclusion of these rehabilitation professionals may have been helpful include (1) commenting on the use of clinically accessible outcomes such as the Functional Independence Measure in the inpatient (instead of the outpatient) arena and (2) the utility of an occupational therapist in improving upper arm dexterity. Citations for rehabilitation studies focused on upper extremities are included in table e-1 at Neurology.org/cp.

In addition to this lack of specialist diversity, the AAN systematic review also presents an incomplete review of the evidence published, perhaps because the AAN review paradigm is geared more towards grading studies of pharmacologic agents. Research methodologies in rehabilitation are less robust than those of therapeutics, and Class I evidence is difficult to obtain in rehabilitation studies because of obstacles to conducting placebo-controlled, double-blind studies. Some data were likely not cited due to a weak level of evidence, and other studies were excluded if they had no control group or fewer than 20 participants. Although it was published in late 2015, this systematic review only covered literature up to 2013, thus not including relevant studies published in the last 3 years.

Despite these criticisms, we laud the authors for reviewing the important topic of the role of rehabilitation in MS and highlighting the need for further research in this area. Without a doubt, data for rehabilitation in MS are not as robust as those for DMTs. It is important to point out that the absence (or relative lack) of high-quality evidence does not prove lack of effect, as suggested in the initial definition of evidence-based medicine (EBM). EBM is “the conscientious, explicit, and judicious use of current best evidence in making decisions about the care of an individual patient.”³ To be most effective, it requires “integrating individual clinical expertise with the best available external clinical evidence from systematic research”³; therefore, it follows that both clinical acumen and comprehensive quality evidence are necessary components to EBM.

As previously stated by one of the authors of this AAN systematic review, “rehabilitation [is] still the only way to improve function in multiple sclerosis.”⁴ The Consortium of MS Centers (CMSC) has long been a platform for multiple medical disciplines to share evidence and treatment strategies and to enhance the care of people with MS, and the International Organization of Multiple Sclerosis Rehabilitation Therapists (IOMSRT) is its rehabilitation arm. This multidisciplinary collaborative effort recently published “Advances in Multiple Sclerosis: A Practical Guide to Rehabilitation in Multiple Sclerosis” (cmeaims.org/rehab-primer-cme.php), which provides specific information about various rehabilitation strategies, mobility assessments, adaptive/assistive devices, cognitive impairment, speech/language interventions, and general health and wellness issues in MS.⁵ In brief, it is believed that rehabilitation favorably influences not only symptoms of MS but also functional mobility, activities of daily living, and participation in vocational and social activities. For example, various rehabilitation interventions have been shown to improve balance,^{6–8} walking speed and endurance,^{9–11} aerobic capacity,^{11,12} strength of the extremities,¹² functional independence,¹³ and quality of life.¹⁴ Rehabilitation strategies have also been shown to decrease falls,^{6,15} fatigue,^{8,12,14,16,17} and overall disability.¹⁸ Generally, cognition^{19–22} and mood²³ have been shown to improve with rehabilitation. A recent systematic review reported some evidence that memory rehabilitation is effective for people with MS; however, some of the included studies were found to have a high risk of bias related to methodology used.²⁴ Rehabilitation studies for common symptoms in MS are presented in table e-1.

Despite our disagreement with the degree of evidence supporting rehabilitation in MS, we agree that larger studies with better research methodologies and higher-quality evidence are needed in rehabilitation. Similar to studies of the DMTs, questions regarding the length of the study and the appropriateness of rating scales such as the Expanded Disability Status Scale (EDSS) are relevant in studies of rehabilitation; of note, many of the studies in the systematic review included individuals with ambulatory dysfunction (some requiring an assistive device),

a range in which the EDSS may not be sufficiently sensitive. Additional issues that potentially confound studies in research include variability in patient effort and the therapeutic intervention utilized. Finally, there are considerable barriers to designing multidisciplinary, double-blind, randomized placebo-controlled studies with large sample sizes in rehabilitation, especially as funding for rehabilitative studies is typically limited.

The AAN systematic review could have, to a greater extent, highlighted the problems created by these methodologic issues and barriers to higher-level research in rehabilitation and argued for solutions that may ultimately influence funding agencies. The question is how to fulfill this need for well-designed trials in rehabilitation. Organizations such as the AAN, CMSC, and IOMSRT have a role in developing and disseminating clearly defined interventions, appropriate endpoints, and effective outcome measures. Collaboration with organizations specific to neurologic rehabilitation, such as the American Physical Therapy Association's Neurology Section, the American Occupational Therapy Association, and the American Speech-Language-Hearing Association, may help enhance and expand MS-specific rehabilitation research currently being performed by rehabilitation scientists and exercise physiologists. Standardized protocols and validated endpoints are needed for all larger studies, especially ones involving multiple centers. It is essential to formulate well-designed trials of rehabilitation therapies and techniques, and to overcome the major challenges of having a placebo group and blinding participants in rehabilitation studies.

Finally, there is the concern that the findings of this systematic review will inhibit the integration of comprehensive, multidisciplinary care into treatment plans for MS. This may occur as a result of external forces limiting access or reimbursement of rehabilitation due to a misinterpretation of this review and an underestimation of the positive effects of rehabilitation for persons living with MS. A recent survey of the North American Research Committee on MS supports long-held concerns that the payer industry can adversely affect access to MS DMTs; it seems reasonable to assume that these restrictions also exist (and perhaps to a greater extent) in regards to rehabilitative services, especially as the evidence base of these interventions is less.²⁵ The patient information sheet of this review also has the potential to limit an individual's decision to participate in rehabilitation, as it suggests that the evidence supporting these interventions is limited. Either way, this will lead to greater underutilization of rehabilitation in MS, leading to unfavorable outcomes for individuals with MS and arguably lower reimbursements for neurologists and rehabilitation professionals caring for them in the upcoming outcome-based reimbursement paradigm. The need for well-designed research trials of rehabilitation in MS remains ongoing and imperative.

REFERENCES

1. Rae-Grant A, Bennett A, Sanders AE, Phipps M, Cheng E, Bever C. Quality improvement in neurology: multiple sclerosis quality measures: executive summary. *Neurology* 2015;85:1904–1908.
2. Haselkorn JK, Hughes C, Rae-Grant A, et al. Summary of comprehensive systematic review: rehabilitation in multiple sclerosis: report of the Guideline Development, Dissemination, and Implementation Subcommittee of the American Academy of Neurology. *Neurology* 2015;85:1896–1903.
3. Sackett DL, Rosenberg WM, Gray JA, Haynes RB, Richardson WS. Evidence based medicine: what it is and what it isn't. *BMJ* 1996;312:71–72.
4. Kraft GH. Rehabilitation still the only way to improve function in multiple sclerosis. *Lancet* 1999;354:2016–2017.
5. Bennett SE, Bednarik P, Bobryk P, Smith C. A Practical Guide to Rehabilitation in Multiple Sclerosis. 2015. Available at: cmeaims.org/rehab-primer-cme.php. Accessed February 24, 2016.
6. Cattaneo D, Jonsdottir J, Zocchi M, Regola A. Effects of balance exercises on people with multiple sclerosis: a pilot study. *Clin Rehabil* 2007;21:771–781.
7. Nilsagård YE, von Koch LK, Nilsson M, Forsberg AS. Balance exercise program reduced falls in people with multiple sclerosis: a single-group, pretest-posttest trial. *Arch Phys Med Rehabil* 2014;95:2428–2434.
8. Hebert JR, Corboy JR, Manago MM, Schenkman M. Effects of vestibular rehabilitation on multiple sclerosis-related fatigue and upright postural control: a randomized controlled trial. *Phys Ther* 2011;91:1166–1183.

9. Van den Berg M, Dawes H, Wade DT, et al. Treadmill training for individuals with multiple sclerosis: a pilot randomised trial. *J Neurol Neurosurg Psychiatry* 2006;77:531–533.
10. Dettmers C, Sulzmann M, Ruchay-Plössl A, Güntler R, Vieten M. Endurance exercise improves walking distance in MS patients with fatigue. *Acta Neurol Scand* 2009;120:251–257.
11. Rampello A, Franceschini M, Piepoli M, et al. Effect of aerobic training on walking capacity and maximal exercise tolerance in patients with multiple sclerosis: a randomized crossover controlled study. *Phys Ther* 2007;87:545–555.
12. Petajan JH, Gappmaier E, White AT, Spencer MK, Mino L, Hicks RW. Impact of aerobic training on fitness and quality of life in multiple sclerosis. *Ann Neurol* 1996;39:432–441.
13. Solari A, Filippini G, Gasco P, et al. Physical rehabilitation has a positive effect on disability in multiple sclerosis patients. *Neurology* 1999;52:57–62.
14. Dalgas U, Stenager E, Ingemann-Hansen T. Multiple sclerosis and physical exercise: recommendations for the application of resistance-, endurance- and combined training. *Mult Scler* 2008;14:35–53.
15. Sosnoff JJ, Moon Y, Wajda DA, et al. Fall risk and incidence reduction in high risk individuals with multiple sclerosis: a pilot randomized control trial. *Clin Rehabil* 2015;29:952–960.
16. George S, White J. Strong evidence exists that multidisciplinary rehabilitation and fatigue management courses improve function and participation in people with multiple sclerosis. *Aust Occup Ther J* 2014;61:288–289.
17. Asano M, Berg E, Johnson K, Turpin M, Finlayson ML. A scoping review of rehabilitation interventions that reduce fatigue among adults with multiple sclerosis. *Disabil Rehabil* 2015;37:729–738.
18. Wier LM, Hatcher MS, Triche EW, Lo AC. Effect of robot-assisted versus conventional body-weight-supported treadmill training on quality of life for people with multiple sclerosis. *J Rehabil Res Dev* 2011;48:483–492.
19. Pepping M, Brunings J, Goldberg M. Cognition, cognitive dysfunction, and cognitive rehabilitation in multiple sclerosis. *Phys Med Rehabil Clin N Am* 2013;24:663–672.
20. Kalron A, Zeilig G. Efficacy of exercise intervention programs on cognition in people suffering from multiple sclerosis, stroke and Parkinson's disease: a systematic review and meta-analysis of current evidence. *NeuroRehabilitation* 2015;37:273–289.
21. Santos T, Pinheiro J, Barros P. Cognitive impairment in multiple sclerosis. *Eur Neurol Rev* 2015;10:157.
22. Sandroff BM, Hillman CH, Benedict RH, Motl RW. Acute effects of walking, cycling, and yoga exercise on cognition in persons with relapsing-remitting multiple sclerosis without impaired cognitive processing speed. *J Clin Exp Neuropsychol* 2015;37:209–219.
23. Ensari I, Sandroff BM, Motl RW. Effects of single bouts of walking exercise and yoga on acute mood symptoms in people with multiple sclerosis. *Int J MS Care* 2016;18:1–8.
24. Das Nair R, Martin KJ, Lincoln NB. Memory rehabilitation for people with multiple sclerosis. *Cochrane Database Syst Rev* 2016;3:CD008754.
25. Wang G, Marrie RA, Salter AR, et al. Health insurance affects the use of disease-modifying therapy in multiple sclerosis. *Neurology* 2016;87:365–374.

Received April 18, 2016. Accepted in final form October 6, 2016.

AUTHOR CONTRIBUTIONS

M.H. Sutliff: drafting/revising the manuscript, acquisition of data. S.E. Bennett: drafting/revising the manuscript. P. Bobryk: drafting/revising the manuscript. J. Halper: drafting/revising the manuscript. L.A. Saslow: drafting/revising the manuscript. L.T. Skutnik: drafting/revising the manuscript. C. Smith: drafting/revising the manuscript. K. Zackowski: drafting/revising the manuscript, study concept or design. D.E. Jones: drafting/revising the manuscript, analysis or interpretation of data.

ACKNOWLEDGMENT

The following organizations reviewed this position statement and endorse this work: Consortium of Multiple Sclerosis Centers, International Organization of MS Nurses, and International Organization of MS Rehabilitation Therapists.

STUDY FUNDING

Funding provided by the Consortium of Multiple Sclerosis Centers (CMSC).

DISCLOSURES

M.H. Sutliff serves on a scientific board and speakers' bureau for and has received funding for travel and/or speaker honoraria from Acorda Therapeutics and receives royalties from Geauga Rehabilitation Engineering for sales of the Hip Flexion Assist Device. S.E. Bennett serves on a scientific board and speakers' bureau for and has received funding for travel and/or speaker honoraria from Acorda Therapeutics and serves on an advisory board for EMD Serono. P. Bobryk has received funding for travel and/or speaker honoraria from Consortium of MS Centers, MS Foundation, and Can Do Multiple Sclerosis. J. Halper serves on the editorial board of *International Journal of MS Care* and is CEO of Consortium of MS Centers and receives publishing royalties for *Nursing Care in Multiple Sclerosis: A Core Curriculum* (Springer Medical Publishing, 2011). L.A. Saslow serves as a consultant to Consortium of MS Centers. L.T. Skutnik has served as a consultant for and received funding for travel from Biogen. C. Smith holds stock/stock options in Teva and is author on a rehabilitation primer produced by the France Foundation. K. Zackowski serves on the board for and receives honoraria from the Consortium of MS Centers; has received funding for travel or speaker honoraria from ReWalk Robotics and receives research support from Acorda Therapeutics, Minoryx Therapeutics, and National MS Society. D.E. Jones receives salary support from Consortium of Multiple Sclerosis Centers (NARCRMS); has received funding for travel or speaker honoraria from MS Foundation, Multiple Sclerosis Association of America, Consortium of MS Centers, American Academy of Neurology, and Can Do MS; has served as a consultant for Biogen, Novartis, and Pharmacy Quality Alliance; and receives research support from Biogen, National MS Society, and University of Virginia. Full disclosure form information provided by the authors is available with the **full text of this article at Neurology.org/cp**.

Related articles from AAN physician and patient resources

Neurology® ● Neurology.org

Let's rehabilitate cognitive rehabilitation in multiple sclerosis

December 10, 2013;81:2060-2061.

Neurology® Neuroimmunology & Neuroinflammation

Pharmacogenomic study in patients with multiple sclerosis: Responders and nonresponders to IFN-β

October 2015;2:e154.

CB1 receptor affects cortical plasticity and response to physiotherapy in multiple sclerosis

December 2014;1:e48.

Continuum® ● ContinuumJournal.com

Symptom Management and Lifestyle Modifications in Multiple Sclerosis

June 2016;22:815-836.

Neurology Now® ● Neurologynow.com

Healing Tails: Service and therapy dogs can transform the lives of people with neurologic conditions such as epilepsy, autism, and multiple sclerosis. Dog owners and other experts explain how.

February/March 2016;12:46-55.

Neurology Today® ● Neurotodayonline.com

INSIDE THE AAN SECTIONS: The Multiple Sclerosis Section — Navigating Escalating Costs and New Treatment Frontiers

February 19, 2015;15:22-25.

Neurology® Clinical Practice

Rehabilitation in multiple sclerosis: Commentary on the recent AAN systematic review

Matthew H. Sutliff, Susan E. Bennett, Patricia Bobryk, et al.

Neurol Clin Pract 2016;6:475-479 Published Online before print October 27, 2016

DOI 10.1212/CPJ.0000000000000318

This information is current as of October 27, 2016

| | |
|---|--|
| Updated Information & Services | including high resolution figures, can be found at: http://cp.neurology.org/content/6/6/475.full.html |
| Supplementary Material | Supplementary material can be found at: http://cp.neurology.org/content/suppl/2016/10/27/CPJ.000000000000318.DC1 |
| References | This article cites 24 articles, 4 of which you can access for free at: http://cp.neurology.org/content/6/6/475.full.html#ref-list-1 |
| Citations | This article has been cited by 1 HighWire-hosted articles: http://cp.neurology.org/content/6/6/475.full.html#otherarticles |
| Subspecialty Collections | This article, along with others on similar topics, appears in the following collection(s): All Rehabilitation http://cp.neurology.org/cgi/collection/all_rehabilitation Gait disorders/ataxia http://cp.neurology.org/cgi/collection/gait_disorders_ataxia Motor Control http://cp.neurology.org/cgi/collection/motor_control Multiple sclerosis http://cp.neurology.org/cgi/collection/multiple_sclerosis Patient safety http://cp.neurology.org/cgi/collection/patient__safety |
| Permissions & Licensing | Information about reproducing this article in parts (figures, tables) or in its entirety can be found online at: http://cp.neurology.org/misc/about.xhtml#permissions |
| Reprints | Information about ordering reprints can be found online: http://cp.neurology.org/misc/addir.xhtml#reprintsus |

Neurol Clin Pract is an official journal of the American Academy of Neurology. Published continuously since 2011, it is now a bimonthly with 6 issues per year. Copyright © 2016 American Academy of Neurology. All rights reserved. Print ISSN: 2163-0402. Online ISSN: 2163-0933.

