

REVIEW ARTICLE

Evidenced-Based Cognitive Rehabilitation for Persons With Multiple Sclerosis: A Review of the Literature

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ABSTRACT. O'Brien AR, Chiaravalloti N, Goverover Y, DeLuca J. Evidenced-based cognitive rehabilitation for persons with multiple sclerosis: a review of the literature. *Arch Phys Med Rehabil* 2008;89:761-9.

Objectives: To conduct evidence-based review of cognitive rehabilitation intervention research conducted in persons with multiple sclerosis (MS), to classify level of evidence, and to generate recommendations for interventions in this area.

Data Sources: An open (no year limits set) search of Medline, PsychInfo, and CINAHL (eliminating repetitions) using combinations of the following terms: *attention, awareness, cognition, cognitive, communication, executive, executive function, language, learning, memory, perception, problem solving, reasoning, rehabilitation, remediation, training, and working memory*. Reference sections of articles found through the sites were also searched.

Study Selection: Studies were chosen based on criteria from previous evidence-based reviews such that articles are excluded from the review if (1) the study was not an intervention, (2) it was a theoretic article, (3) it was a review article, (4) detail was lacking to fully evaluate the intervention, (5) it was not MS-specific, (6) it included a pediatric sample, (7) it was a case report without empirical data to evaluate outcomes, (8) it was not peer-reviewed (also excludes book chapters), (9) it was a pharmacologic intervention, or (10) it was not available for review in English.

Data Extraction: Articles were categorized into interventions for attention, learning and memory, executive functioning, or nonspecified/combined cognitive domains. There were 4 reviewers in the current study. All articles were reviewed independently by at least 2 persons and abstracted according to predetermined criteria. There was a final total of 16 articles, which underwent a full review and classification of a level of evidence based on previously published peer-reviewed methodology used for evidence-based reviews.

Data Synthesis: The current review yielded 16 studies of cognitive rehabilitation for persons with MS, including 4 class I studies, 5 class II studies, 2 class III studies, and 5 class IV studies. Two intervention methodologies in the area of verbal

learning and memory received support for a practice guideline and practice option, respectively.

Conclusions: Cognitive rehabilitation in MS is in its relative infancy. More methodologically rigorous research is needed to determine the effectiveness and efficacy of various cognitive rehabilitation interventions. Specific recommendations for future research are given.

Key Words: Cognition disorders; Cognitive therapy; Multiple sclerosis; Practice guideline; Rehabilitation; Review [publication type].

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MULTIPLE SCLEROSIS (MS), a progressive disease of the central nervous system, is characterized by the production of widespread lesions, or plaques, in the brain and spinal cord. As a result of the widespread nature of the myelin plaques and axonal injuries, MS results in a wide symptom array, including motor, cognitive, and neuropsychiatric problems,¹ with high variability in presenting symptoms and disease course.² Reaching a definitive diagnosis of MS can be challenging and is done through various procedures including taking medical history, description of symptoms, neuroimaging of the brain and spinal cord, cerebrospinal fluid collection, and measurement of evoked responses. To be given a diagnosis of MS, a person must have had at least 2 distinct episodes of symptomatology separated by at least 1 month and must have lesions in more than 1 area of the brain or spinal cord. It is challenging to diagnose MS with certainty because of the variety of symptoms involved and the varying disease courses. Because the physical symptoms are most often focused on for diagnosis, cognitive functioning may less frequently be assessed or included in an immediate focus of treatment.

Cognitive impairment is common in MS, with current prevalence rates ranging from 43% to 70%.^{3,4} MS has been shown to negatively affect various aspects of cognitive functioning including attention,^{5,6} information processing abilities^{5,7} (including processing speed⁸⁻¹¹), new learning,^{12,13} and memory functioning.¹

Cognitive impairments are associated with reduced functional status in MS.^{14,15} Cognitive impairment often has a deleterious impact on someone's personal, occupational, and social functioning, as well as overall quality of life (QOL).¹⁵ For example, Rao et al¹⁶ found that people with MS who have cognitive impairments—as opposed to those with a purely physical disability—were less likely to be employed, were engaged in fewer social and vocational activities, had greater difficulties in carrying out routine household tasks, and were more vulnerable to psychiatric illness. Given the significant effect that deficits in cognitive functioning have on the QOL of persons with MS, the alleviation of such deficits should be a major goal of MS research and practice.

Cognitive and behavioral rehabilitation are designed to enhance a person's capacity to process and interpret information and to improve his/her ability to function in all aspects of

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family and community life.¹⁷ Despite the need for cognitive rehabilitation services as a standard of care, there is a paucity of research studies designed to investigate treatment approaches or their effectiveness in persons with MS.¹⁸⁻²⁰ The few existing cognitive rehabilitation programs within MS have been aimed at improving attentional deficits,²¹ communication skills,²² and memory functioning.²³⁻²⁵ However, most of the existing studies suffer from significant methodologic flaws including small sample size, short follow-up periods, and lack of specific outcome criteria to determine improvement. As a result, researchers and clinicians experience difficulty drawing firm conclusions regarding effectiveness,²⁶ and evidence of effectiveness is ambiguous and controversial.²⁷ Although some studies^{24,25,28-30} exist showing a benefit of cognitive rehabilitation for persons with MS, others^{31,32} have failed to show a benefit. An expert review panel recently underscored the need for cognitive rehabilitation interventions for persons with MS²⁷ and recommended strategies such as cognitive structuring, substitution strategies, use of compensatory devices, and mnemonic approaches. The current study is the first, to our knowledge, to conduct a comprehensive evidence-based review of the existing cognitive rehabilitation intervention literature specifically within MS.

To date, most of the work on rehabilitation techniques for cognitive impairments has been done with stroke or head-injured patients.²⁶ The current clinical environment requires that therapeutic interventions be supported by class I evidence (eg, randomized controlled trials).³³ The current study reviews the existing cognitive rehabilitation literature in MS to accurately describe the current status of the field, offering practice guidelines for clinicians and spurring interest and providing direction for ongoing MS research.

METHODS

We conducted a comprehensive review of research studies that have focused on cognitive rehabilitation interventions for persons with MS, and as such, relevant literature was identified and reviewed. We implemented methodology used in previous evidence-based reviews.^{34,35} As such, open-dated literature reviews were conducted in Medline, PsychInfo, and CINAHL using the combination of the search terms, which included *attention, awareness, cognition, cognitive, communication, executive, executive function, language, learning, memory, perception, problem solving, reasoning, rehabilitation, remediation, training, and working memory*. Reference sections of selected articles were reviewed to identify any additional relevant studies. The literature search and reference section review yielded an initial list of 224 citations. Articles were eliminated according to previously published criteria.^{34,35} Specifically, a study was eliminated if (1) it was not an intervention, (2) it was a theoretic article, (3) it was a review article, (4) detailed empirical outcomes were not available for evaluation of intervention, (5) the article included populations other than MS, (6) it included a pediatric sample, (7) a case report did not include empirical data to evaluate outcomes, (8) it was not peer-reviewed, (9) it was a pharmacologic intervention, or (10) the article was not available for review in English. On initial review of the citations, 19 articles were identified as research interventions studies of cognitive rehabilitation in MS.

The 19 articles were randomly assigned to the 4 reviewers who conducted this study. No one reviewed a study on which he/she was an author. Each study was reviewed independently by 2 people who rated it for level of evidence and completed a review table (1) to characterize important elements of each study, (2) to describe the cognitive domain(s) targeted, (3) to

Table 1: Levels of Evidence

Level	Criteria
Class I	<ul style="list-style-type: none"> Well-designed, prospective, randomized controlled trials
Class Ia	<ul style="list-style-type: none"> Well-designed, prospective quasi-randomized assignment to treatment conditions (eg, alternating conditions)
Class II	<ul style="list-style-type: none"> Prospective, nonrandomized cohort studies Retrospective, nonrandomized case-control studies Clinical series with well-designed controls that permitted between-subjects comparisons of treatment conditions All other controlled studies in a representative population
Class III	<ul style="list-style-type: none"> Clinical series without concurrent controls Studies reporting 1 or more case study that used appropriate single-subject methods (eg, multiple baselines)
Class IV	<ul style="list-style-type: none"> Evidence from uncontrolled studies, case series, case reports, or expert opinion

NOTE. Adapted from Cicerone et al.³⁵ © 2000 by the American Congress of Rehabilitation Medicine and the American Academy of Physical Medicine and Rehabilitation.

describe the sample, and (4) to describe the intervention, outcomes, and evidence of treatment effectiveness.

Decisions for level of evidence were based on standards published by the American Association of Neurologic Surgeons³⁶ for classification of research studies and the classifications described by Cicerone et al.^{34,35} (table 1). Final acceptance of evidence classification was based on total agreement between the 2 reviewers. An a priori decision was made that if there was a discrepancy in the level of evidence assigned for each article, a third reviewer, blinded to the judgments of the first 2 reviewers, would evaluate the article to reach a conclusion for assignment of level of evidence. A third-party reviewer was never needed.

A closer inspection of the full articles by the reviewers showed that 3 of the initial 19 identified articles did not meet the aforementioned inclusion criteria for this review. Of the 3 eliminated articles, 2 were theoretic articles that described general approaches to cognitive rehabilitation; the other article qualitatively described cognitive rehabilitation approaches used at rehabilitation facility, without any accompanying data or specific outcomes. This resulted in a final total of 16 articles that underwent a full review and classification of a level of evidence (table 2).

After review of the article and classification of level of evidence, reviewers then provided recommendations based on the strength of the levels of evidence found in the research as to the feasible and preferable approaches to cognitive rehabilitation. The recommendations were classified as either (1) practice standards, (2) practice guidelines, or (3) practice options, based on the body of evidence available.^{34,35} See appendix 1 for the guidelines used in deciding on the appropriate recommendation for each domain.

RESULTS

Attention

Two studies focused specifically on the remediation of attention skills. Two additional studies had an attention remediation component in addition to components for other cognitive skills. Of the 4 studies in this area, there was 1 class I study

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