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REVIEW ARTICLE (META-ANALYSIS)

Evidenced-Based Cognitive Rehabilitation for Persons With Multiple Sclerosis: An Updated Review of the Literature From 2007 to 2016

Yael Goverover, PhD,[a,b] Nancy D. Chiaravalloti, PhD,[b,c] Amanda R. O'Brien, PhD,[b] John DeLuca, PhD[b,c,d]

From the [a]Department of Occupational Therapy, New York University, New York, NY; [b]Kessler Foundation, East Hanover, NJ; [c]Department of Physical Medicine and Rehabilitation, Rutgers University — New Jersey Medical School, Newark, NJ; and [d]Department of Neurology and Neurosciences, Rutgers University — New Jersey Medical School, Newark, NJ.

Abstract

Objective: To update the clinical recommendations for cognitive rehabilitation of people with multiple sclerosis (MS), based on a systematic review of the literature from 2007 through 2016.

Data Sources: Searches of MEDLINE, PsycINFO, and CINAHL were conducted with a combination of the following terms: *attention*, *awareness*, *cognition*, *cognitive*, *communication*, *executive*, *executive function*, *language*, *learning*, *memory*, *perception*, *problem solving*, *reasoning*, *rehabilitation*, *remediation*, *training*, *processing speed*, and *working memory*. One hundred twenty-nine articles were identified and underwent initial screening.

Study Selection: Fifty-nine articles were selected for inclusion after initial screening. Nineteen studies were excluded after further detailed review. Forty studies were fully reviewed and evaluated.

Data Extraction: Articles were assigned to 1 of 6 categories: attention, learning and memory, processing speed and working memory, executive functioning, metacognition, or nonspecified/combined cognitive domains. Articles were abstracted and levels of evidence were decided using specific criteria.

Data Synthesis: The current review yielded 6 class I studies, 10 class II studies, and 24 class III studies. One intervention in the area of verbal learning and memory received support for a practice standard, 2 computer programs received support as practice guidelines (in the area of attention and multicognitive domains), and several studies provided support for 5 practice options in the domains of attention and learning and memory.

Conclusions: Substantial progress has been made since our previous review regarding the identification of effective treatments for cognitive impairments in persons with MS. However, much work remains to be done to optimize rehabilitation potential by applying the most methodologically rigorous research designs to provide class I evidence in support of a given treatment strategy.

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The first systematic review of cognitive rehabilitation (CR) interventions for people with multiple sclerosis (MS) found only 16 reported studies that were conducted specifically in the MS population.[1] Six of these studies focused on the remediation of learning and memory, whereas a few focused on attention and unspecified or multiple skills. At that time, only 2 interventions in the area of verbal learning and memory received support for a practice guideline and a practice option. The reviewers recommended that more methodologically rigorous research was needed, especially in the areas of processing speed, attention, and executive function.

Since this original article in 2008, several reviews of CR in persons with MS have been conducted. For instance, a recent systematic review[2] that included studies published through January 2014 identified 33 articles using PubMed and Web of Science. Authors concluded that although earlier articles concentrated on memory and skill acquisition, more recent studies

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shifted their focus to executive function, attention, and processing speed. However, these findings were insufficient to support new practice options, guidelines, or standards.

In the most recent Cochrane review on memory rehabilitation in MS,[3] there was good evidence reported to support the effectiveness of memory rehabilitation on memory function and quality of life. However, the authors criticized the findings of the reviewed studies and called for robust randomized controlled trials (RCTs) with rigorous methodologic standards and better quality of reporting, using ecologically valid outcome assessments to measure generalizability of treatments.

The current systematic review was conducted as a follow-up to our previous systematic review of CR in MS[1] and the most recent reviews.[2,3] We provide current classification of levels of evidence in support of currently available CR techniques for persons with MS. Only articles published after our original study (ie, articles published after 2007) were reviewed in this article. We additionally evaluated whether new practice options, guidelines, or standards could be added to the ones that were previously recommended.[1] Therefore, articles from our original review[1] were taken into consideration when making current decisions regarding practice recommendations, specifically noting if the newer outcomes conflicted with or provided additional support from the previous work. This new review also examined whether the field has experienced a shift in the focus of interventions and outcome to document CR efficacy.

Methods

A systematic review of treatment studies on CR for persons with MS was performed in several steps, following methodology used in previous evidence-based reviews.[1,4] First, literature searches were conducted using the following databases: PubMed, PsycINFO, MEDLINE, and CINAHL. The following terms were used in the searches: *cognitive rehabilitation* or *cognitive remediation*, in combination with *multiple sclerosis*, *attention*, *awareness*, *cognition*, *cognitive*, *communication*, *executive*, *executive function*, *language*, *learning*, *memory*, *perception*, *problem solving*, *reasoning*, *remediation*, *training*, *processing speed*, and *working memory*. The search was limited to studies published in English with human participants that were published between January 2007 and March 2016. Articles were excluded if (1) the study was not an intervention, (2) the study was not an empirical study, (3) the publication was a review article, (4) >50% of the participants did not have MS, (5) the study focused on a pediatric sample, (6) the publication was a case report without empirical data to evaluate outcomes, (7) the article was not peer reviewed (eg, book chapters), (8) the intervention was not targeting a cognitive domain, (9) the intervention under investigation was pharmacologic, or (10) the intervention under investigation was cognitive behavioral therapy for the treatment of psychological symptoms rather than cognition. These exclusion criteria were designed to be consistent with previous reviews of the CR literature.[1,4] The initial search yielded 129 articles. These initially identified 129 article abstracts and titles were reviewed and screened based on the aforementioned exclusion criteria by 2 members of the study team (Y.G. and N.D.C.). In this process, 70 articles were excluded (fig 1); 59 articles were therefore selected for a full review. These 59 identified studies were divided among the authors of this article with one restriction: a reviewer cannot evaluate his or her own article. Each study was reviewed independently by 2 authors who rated it for level of evidence via a structured review table.

The review table was used to extract the following information for each study: purpose of the study and description of the intervention, targeted cognitive domains, sample size, inclusion of a screening for impairment in some aspect of cognition, study results, and what type of outcome was used to document efficacy and generalization. During this process, an additional 19 articles were excluded for the following reasons: (1) 12 were follow-up studies (ie, studies that included the same participants as the original study but reported on a different outcome variable, studies reporting post hoc data analyses); (2) 1 study did not evaluate a cognitive intervention, but cognitive behavioral therapy; (3) 1 study used only 1 participant with MS and most participants had a stroke; and (4) 5 studies assessed the feasibility of treatment or adherence to the treatment offered, without evaluating treatment efficacy. Therefore, 40 articles were included in the final review. The fully reviewed articles were then classified based on level of evidence. Decisions for classifications of evidence were based on standards published for therapeutic trials by the American Academy of Neurology (AAN)[5] (table 1). Potential bias for individual study or study quality was assessed using the AAN criteria and the Physiotherapy Evidence Database index. It was required that the 2 reviewers independently agreed on the level of evidence for each included study. If the 2 initially assigned reviewers disagreed regarding the level of evidence (as occurred for 5 articles), a third reviewer, blinded to the decision of the first 2 reviewers, established the conclusion. After review of the articles and classification of level of evidence, reviewers then provided recommendations regarding the strength of evidence found in the research and recommendations for practice. The recommendations were described in appendix 1 as practice standards, practice guidelines, or practice options based on the body of evidence available.[4]

List of abbreviations:

AAN	**American Academy of Neurology**
APT	**attention process training**
CR	**cognitive rehabilitation**
GAS	**goal attainment scaling**
MS	**multiple sclerosis**
mSMT	**modified Story Memory Technique**
RCT	**randomized controlled trial**

Results

Forty articles published between January 2007 and November 2016 were selected to be included in this review. Studies were classified according to (1) participants (type of MS targeted and whether the targeted cognitive domain was impaired), (2) cognitive training characteristics (method of intervention: technology: computer program, video games, or cognitive or behavioral based; dosage: duration and frequency), (3) domain targeted (ie, memory, attention), and (4) outcome evaluated (eg, cognitive, functional; long term vs immediate).

Attention

Two class I and 1 class III studies examined the efficacy of programs related to only attention. Note that several studies included in this review evaluated programs that addressed attention within a more complex treatment that also targeted additional cognitive