Title: Evidence-Based Cognitive Rehabilitation: Systematic Review of the Literature From 2009 Through 2014.

Authors: Keith D. Cicerone, PhD[1,2], Yelena Goldin, PhD[1,2], Keith Ganci, PhD[3], Amy Rosenbaum, PhD[4], Jennifer V. Wethe[5], PhD., Donna M. Langenbahn, PhD[6,7], James F. Malec, PhD[5,9], Thomas F. Bergquist, PhD[5], Kristine Kingsley, PsyD[6,7], Drew Nagele, PsyD[10,11], Lance Trexler, PhD[8,9], Michael Fraas, PhD[12], Yelena Bogdanova, PhD[13,14], J. Preston Harley, PhD[15].

Affiliations:

1. JFK Johnson Rehabilitation Institute, Hackensack Meridian Health System
2. Rutgers Robert Wood Johnson Medical School
3. Charlotte Center for Neuropsychological Services
4. Park Terrace Care Center
5. Mayo Clinic College of Medicine and Science
6. Rusk Rehabilitation at NYU Langone Health
7. New York University School of Medicine
8. Rehabilitation Hospital of Indiana
9. Indiana University School of Medicine
10. Beechwood NeuroRehab
11. Philadelphia College of Osteopathic Medicine
12. Western Washington University
13. Boston University School of Medicine
14. VA Boston Healthcare System

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15. Advocate Christ Medical Center

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Corresponding Author: Keith D. Cicerone, Ph.D.

JFK Johnson Rehabilitation Institute

2048 Oak Tree Road

Edison, NJ 08820

(732) 906-2640

Keith.Cicerone@hackensackmeridian.org

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TITLE

Evidence-based cognitive rehabilitation: Systematic review of the literature from 2009 through 2014.

ABSTRACT

Objective: To conduct an updated, systematic review of the clinical literature, classify studies based on the strength of research design, and derive consensual, evidence-based clinical recommendations for cognitive rehabilitation of people with TBI or stroke.

Data Sources: Online Pubmed and print journal searches identified citations for 250 articles published from 2009 through 2014.

Study Selection: 186 articles were selected for inclusion after initial screening. 50 articles were initially excluded (24 healthy, pediatric or other neurologic diagnoses, 10 non-cognitive interventions, 13 descriptive protocols or studies, 3 non-treatment studies). 15 articles were excluded after complete review (1 other neurologic diagnosis, 2 non-treatment studies, 1 qualitative study, 4 descriptive papers, 7 secondary analyses). 121 studies were fully reviewed.

Data Extraction: Articles were reviewed by CRTF members according to specific criteria for study design and quality, and classified as providing Class I, Class II, or Class III evidence. Articles were assigned to 1 of 6 possible categories (based on interventions for attention, vision and neglect, language and communication skills, memory, executive function, or comprehensive-integrated interventions).

Data Synthesis: Of 121 studies, 41 were rated as Class I, 3 as Class Ia, 14 as Class II, and 63 as Class III. Recommendations were derived by CRTF consensus from the relative strengths of the evidence, based on the decision rules applied in prior reviews.

Conclusions: CRTF has now evaluated 491 papers (109 Class I or Ia, 68 Class II, and 314 Class III) and makes 29 recommendations for evidence-based practice of cognitive rehabilitation (9 Practice Standards, 9 Practice Guidelines and 11 Practice Options). Evidence supports Practice Standards for attention deficits after TBI or stroke; visual scanning for neglect after right hemisphere stroke; compensatory strategies for mild memory deficits; language deficits after left hemisphere stroke; social communication deficits after TBI; metacognitive strategy training for deficits in executive functioning; and comprehensive-holistic neuropsychological rehabilitation to reduce cognitive and functional disability after TBI or stroke.

Key Words: Brain injuries; Stroke; Practice guidelines as topic; Rehabilitation.

LIST OF ABBREVIATIONS

ABI	acquired brain injury
APT	Attention Process Training
BHW	Behavioral Health Workshop
CO-OP	Cognitive Orientation to Occupational Performance
CRTF	Cognitive Rehabilitation Task Force
CVA	cerebrovascular accident
DTI	Diffusion Tensor Imaging
FA	fractional anisotropy
FIM	Functional Independence measure
GMT	Goal Management Training
IOM	Institute of Medicine
MRI	magnetic resonance imaging
MST	metacognitive strategy training
NFT	neurofunctional training
PDA	personal data assistant
PCS	post-concussion symptoms
PM	prospective memory
PST	problem solving therapy
PTSD	post-traumatic stress disorder
RCT	randomized controlled trial
SE	supported employment
SOT	standard occupational therapy

TBI	traumatic brain injury
tDCS	transcranial direct current stimulation
TPM	Time Pressure Management
VR	virtual reality
WM	working memory

The Cognitive Rehabilitation Task Force (CRTF) of the American Congress of Rehabilitation Medicine, Brain Injury Special Interest Group, has previously published three systematic reviews of cognitive rehabilitation after TBI or stroke [1 - 3] Our intent has been to summarize the existing literature in order to provide evidence-based recommendations for the clinical practice of cognitive rehabilitation. We have consistently attempted to base our recommendations on the best available scientific evidence, to be applied in conjunction with clinical judgment and patients' preferences and values. Since our initial efforts there has been a proliferation of reviews of the literature regarding the effectiveness of cognitive rehabilitation. Some of these reviews have maintained a pragmatic, clinical focus while others have emphasized the methodologic rigor of studies and often reached the conclusion that there is insufficient evidence to guide clinical practice. This represents a form of therapeutic nihilism that ignores a basic tenet of evidence-based practice: to utilize the *best available* scientific evidence to support clinical practice. While we support the goals of conducting research of high methodologic quality [4], we continue to believe that the extant evidence allows for the extrapolation of useful clinical recommendations from the scientific literature. The CRTF therefore conducted the current review in order to identify the best available scientific evidence to inform the clinical practice of cognitive rehabilitation. This effort is distinct from most other reviews in its emphasis on the development of practical, evidence-based guidelines, to be used in conjunction with clinical judgment and patient preferences.

The current paper is an updated systematic review of the literature published from 2009 through 2014 addressing cognitive rehabilitation for people with TBI or stroke. We included studies where at least the majority of participants had sustained either traumatic brain injury (mild, moderate or severe) or stroke. Our emphasis on these conditions is based on their clinical prevalence of acquired cognitive deficits and participation in neurorehabilitation, and is consistent with our prior reviews (while other CRTF reviews have addressed other medical conditions). We reviewed and analyzed studies that allowed us to evaluate the effectiveness of behavioral interventions for cognitive limitations. Whenever possible we analyzed studies based on comparisons with alternative non-treatment or alternative treatment conditions. We included a range of outcomes representing physiologic function, subjective report or objective measures of neurocognitive impairments, activity limitations or social participation among participants examined during either acute or post-acute stages of recovery. We integrated these findings in our current practice recommendations.

METHODS

The development of evidence-based recommendations followed our prior methodology for identification of the relevant literature, review and classification of studies, and development of recommendations. These methods are described in more detail in our initial publication.[1] For the current review, online literature searches using PubMed were conducted weekly using the terms cognitive rehabilitation brain injury and cognitive rehabilitation stroke. For our previous reviews we utilized a larger and more diverse set of search terms, and we initially included these terms in our current search strategy. However, early in this process we observed that the broader search terms appeared to have equivalent sensitivity and greater specificity for the identification of relevant citations. We also screened 7 rehabilitation and neuropsychology journals through monthly subscriptions. The references from relevant identified articles were also screened. The use of multiple search methods should assure that a comprehensive search was conducted with little if any systematic bias. Articles were assigned to 1 of 6 possible categories (based on interventions for attention, vision and neglect, language and communication skills, memory, executive function, or comprehensive-integrated interventions) that specifically address the rehabilitation of cognitive disability. For this review we did not include studies of aphasia rehabilitation after stroke, but concentrated on functional communication deficits. We based this decision on the large number of studies addressing aphasia rehabilitation, most of which concerned highly specific linguistic deficits and interventions and were felt to be of limited direct relevance to our current objectives.

Articles were reviewed by 2 CRTF members who completed a Study Review form and abstracted according to specific criteria: subject characteristics (age, education, gender, nature and severity of injury, time postinjury, inclusion/exclusion criteria); treatment characteristics (treatment setting, target behavior or function, nature of treatment, sole treatment or concomitant treatments); methods of monitoring and analyzing change (e.g. change on dependent variable over course of treatment; pretreatment and posttreatment tests on measures related to target behavior; patient, other, or clinician ratings related to target behaviors; change on functional measures; global outcome status); maintenance of treatment effects; statistical analyses performed; and evidence of treatment effectiveness (e.g. improvement on cognitive function being assessed, evidence for generalized improvement on functional outcomes). Each study was classified as providing Class I, Class II, or Class III evidence, as described below. Seven CRTF reviewers were experienced in the process of conducting a systematic review of cognitive rehabilitation studies. An additional 14 reviewers were trained to review and classify articles for the purpose of this systematic review. These reviewers attended at least one in-person training session through the CRTF and achieved consensus with experienced reviewers on at least 4 articles before serving as independent reviewers. In addition to completing the Study Review form, each reviewer also completed a rating of Quality Criteria [4] for each study. This material will be submitted for separate publication.

The CRTF initially identified citations for 250 published articles. We included articles published between 2009 and 2014 inclusive (including articles published electronically through this period); we stopped identifying potential articles on December 15, 2015. The abstracts or complete articles were reviewed in order to eliminate articles according to the following exclusion criteria: (1) nonintervention articles, including nonclinical experimental manipulation, (2) theoretical articles or descriptions of treatment approaches, (3) review articles, (4) articles without adequate specification of interventions, (5) articles that did not include participants primarily with a diagnosis of TBI or stroke, (6) studies of pediatric subjects, (7) single case reports without empirical data, (8) non-peer reviewed articles and book chapters, (9) articles describing pharmacologic interventions, and (10) non-English language articles.

Based upon initial review of abstracts or full articles we eliminated 64 reviews published between 2009 and 2014. We eliminated an additional 50 articles based on other exclusion criteria (17 studies of participants with other neurologic diagnoses, 10 non-cognitive interventions, 8 descriptive studies, 3 non-treatment studies, 5 experimental manipulations with healthy subjects, 5 treatment protocols, 2 pediatric subjects). An additional 8 articles were excluded after complete review (1 with other neurologic diagnosis, 2 non-treatment studies, 1 qualitative study, 2 treatment protocols and 2 descriptive papers). We also identified 7 papers representing secondary analyses (2 imaging findings, 2 analyses of patient characteristics, and 3 follow-up studies of prior RCTs); these 7 papers were not classified based on level of evidence but were used to inform our findings and recommendations.

We fully reviewed and evaluated 121 studies. For these 121 studies, the level of evidence was determined based on criteria used in our prior reviews. [1-3] Well-designed, prospective, RCTs were considered class I evidence; studies using a prospective design with quasi-randomized assignment to treatment conditions were designated as class Ia studies. Given the inherent difficulty in blinding rehabilitation interventions, we did not consider this as criterion for class I or Ia studies, consistent with our prior reviews. Class II studies consisted of prospective, nonrandomized cohort studies; retrospective, nonrandomized case-control studies; or multiple-baseline studies that per- mitted a direct comparison of treatment conditions. Clinical series without concurrent controls, or single-subject designs with adequate quantification and analysis were considered class III evidence. Studies that were designed as comparative effectiveness studies but did not include a direct statistical comparison of treatment conditions were considered class III. Disagreements between the 2 primary reviewers (as occurred for 14 articles) were first addressed by discussion between reviewers to correct minor sources of disagreement, and then by obtaining a third review.

Of the 121 studies included for analysis in the current review, 41 were rated as class I, 3 as class Ia, 14 as class II, and 63 as class III. The overall evidence within each predefined area of intervention was synthesized and recommendations were derived from the relative strengths of the evidence. The level of evidence required to determine Practice Standards, Practice Guidelines, or Practice Options was based on the decision rules applied in our initial review (Table 1). All recommendations were reviewed for consensus by the CRTF through face-to-face discussion.

INSERT TABLE 1 ABOUT HERE

RESULTS

Rehabilitation of Attention

We reviewed 13 studies (5 Class I [5-9], 1 Class II [10] and 7 Class III [11 - 17]) addressing the remediation of attention. Four studies (1 Class I [5], 1 Class II [10], and 2 Class III [11,14]) evaluating direct attention training using APT provide additional evidence that APT can improve performance on training tasks and direct measures of global attention. A Class I study [5] compared APT and standard care for hospitalized stroke patients an average of 18 days after a stroke. Participants who received APT demonstrated greater improvement on a composite measure of attention although broader functional outcomes did not differ. This finding is consistent with existent evidence suggesting limited benefits of APT compared with standard brain injury rehabilitation during acute recovery.

Two studies (one Class II [6], one Class III [11]) utilized single subject designs to investigate the functional benefits of APT as a component of treatment for language deficits. The Class II study used APT-3, which incorporates direct attention training and metacognitive strategy training, to improve reading comprehension in 4 chronic ischemic stroke patients with mild to moderate aphasia [6]. All 4 participants demonstrated improvement on select standardized measures of attention, while modest gains in reading comprehension were obtained by 2 participants. The authors suggest that improvements in allocation of attention and self-monitoring may underlie improvements in reading comprehension although there is limited evidence for transfer of attention training to functional cognition.

Computer-based working memory training. Two Class I studies evaluated whether computer-based working memory training (Cogmed QM) can increase WM performance, and lead to generalized improvements.[7,8] *The* samples in both studies included individuals with mixed acquired brain injuries, a majority with a diagnosis of stroke. In one study, participants demonstrated significant improvement on the trained working memory tasks, untrained working memory tasks, and self-reported cognitive difficulties in everyday living situations, and WM-related occupational performance. [7] The second Class I study investigated WM training in conjunction with standard outpatient rehabilitation, compared with standard rehabilitation alone.[8] Despite isolated benefits on screening measures of attention and higher cognitive functioning for the WM intervention group, there was no difference between groups on an aggregate WM measure or self-rated executive problems after treatment, making it difficult to attribute specific benefits to the WM intervention. There is Class III evidence (including follow-up [18] to a Class I study [8]) suggest generalized improvements in self-reported cognitive problems in daily functioning, fatigue, and occupational performance after WM training with Cogmed.[17, 18]

A Class I study evaluated computer-based WM training (a component of RehaCom) combined with training in semantic structuring and word fluency, compared with "standard memory therapy" focused on learning strategies.[9] WM training resulted in significant improvements on working memory and word fluency, as well as on PM performance, indicating both a direct benefit and generalization of training effects.

Specificity of direct attention training. Vallat-Azouvi and colleagues [15, 16] conducted a number of single-subject studies that addressed the specificity of training for discrete components of working memory impairment (verbal maintenance, visuospatial maintenance, central executive) after TBI or stroke. The results suggest greater efficacy of "modular" training for each component, with less specificity of benefits on self-reported generalization to everyday working memory difficulties. These findings are consistent with the fundamental assumptions of process-specific cognitive training.

Neuroplasticity and direct attention training. Two Class III studies [12, 13] incorporated neuroimaging to investigate whether computer-based attention training (combined with strategy training [12]) can contribute to functional restoration and reintegration of neural networks following brain injury. These studies demonstrated training-induced changes in neuropsychological performance that corresponded with white matter microstructural changes as measured by DTI-derived FA, [12] and redistribution of the cerebral attention network marked by decreased activation of the frontal lobe and increased activation of the anterior cingulate cortices and precuneus. [13]

Metacognitive strategy training. One Class I study of metacognitive strategy training extends findings from an earlier review supporting the effectiveness of TPM, a cognitive strategy used to compensate for mental slowness/slow information processing.[6] The study used a multicenter, randomized, single-blind control trail to investigate the effects of 10 hours of TPM training compared with usual care in a sample of stroke patients at least 3 months post stroke. Participants in both groups showed an improvement in their use of strategies and reported significantly fewer complaints following treatment. However, the TPM group showed significantly greater use of strategies, and at 3-month follow-up, significantly faster task completion indicating greater efficiency in performing everyday tasks.

INSERT TABLE 2 ABOUT HERE

Recommendations. The CRTF has previously recommended that treatment of attention deficits should incorporate both direct attention training and metacognitive strategy training to increase task performance and promote generalization to daily functioning after TBI *(Practice Standard)*. The present results support extending the recommendation to individuals with stroke during the post-acute stages of recovery (Table 2).

Improvements in working memory are evident after training on specific, "modular" components of working memory, whether this is achieved through the use of either computer-based or therapist-administered interventions. The evidence also suggests improvement on patient-reported outcomes of everyday activities after working memory training. [3, 15, 18] Based on this recent evidence, we recommend that direct attention training for specific "modular" impairments in WM, including the use of computer-based interventions, be considered to enhance both cognitive and functional outcomes during post-acute rehabilitation for acquired brain injury (Practice Guideline) (Table 2). This Guideline refines and replaces our previous option for the treatment of global attention impairments through computer based interventions. The CRTF continues to emphasize the importance of therapist involvement and intervention to promote awareness and generalization (e.g., metacognitive strategy training) over the stand-alone use of computer-based tasks.

There continues to be insufficient evidence to indicate differential benefits of direct attention training compared with standard (in-patient) brain injury rehabilitation on functional outcomes during acute recovery from TBI or stroke, although this training may improve specific aspects of attention and there is no indication that the incorporation of direct attention training during acute rehabilitation has negative or adverse effects.

Rehabilitation of Visuospatial Functioning

We reviewed 7 Class I studies [19-25] and 6 Class III [26 – 31] studies in the area of visual functioning, with 10 of these studies addressing the remediation of visual neglect after right hemisphere stroke, consistent with the emphasis of the previous CRTF review. Rehabilitation of neglect through practice in visual scanning after right hemisphere stroke has been a recommended as a Practice Standard, and this receives continued support in the current review. [19,20, 22] More recent research has focused on enhancements of scanning procedures and on alternative procedures. Polanowska and colleagues [19] provided Class I evidence that left hand stimulation improved outcomes of scanning training for left-sided neglect compared to scanning training alone. A Class I study by Pandian and colleagues [23] reported that limb activation with mirror therapy (attempting to move the paretic upper extremity to mimic movements of the nonparetic limb reflected in a mirror on the side of the paretic limb) reduced left neglect compared to a sham treatment in an RCT. This study, and an additional Class III study using contralateral limb activation and arm vibration, [28] support prior evidence suggesting the benefits of forced activation of the affected limb in conjunction with visual scanning training for left neglect. [32]

One study that supports the efficacy of visual scanning failed to show a benefit of adding a divided attention task to single-task visuospatial training for neglect. [20] In a class III study, motor imagery failed to improve performance on most neglect measures. [27]

Although a physical rather than a cognitive intervention, right hemi-field eye patching was found to reduce left visuospatial neglect compared to standard care in an RCT [21] and at an equivalent level to visual scanning training in another RCT. [22] Class III evidence was reported for improving neglect through a pointing exercise, [30] tDCS in addition to scanning training, [29] and a series of interventions that included optokinetic stimulation, prismatic adaptation, and transcutaneous electrical nerve stimulation. [26] The CRTF elects not to provide recommendations regarding these physiological interventions. Two systematic reviews [33, 34] provide additional evidence regarding non-cognitive interventions (e.g. prism adaptation, tDCS, drugs) in the rehabilitation of neglect.

Several studies addressed the application of visuospatial interventions to functional limitations [19], [20] and were unable to document generalization of neglect rehabilitation to functional activities. However, it is very likely that neither study was adequately powered to find an effect on functional measures that are affected by factors other than the direct effect of the treatment studied. One Class III study suggests that cognitive interventions that incorporate skill remediation and metacognitive strategies may facilitate return to driving after TBI or stroke. [31] Two follow-up studies [35, 36] described long term maintenance of the positive effects of driving simulator training on return to driving originally reported in a RCT. [25]

Computerized interventions to expand the visual field in cases of hemianopsia was offered as a Practice Option in the previous EBR based on a single RCT, pending replication. However, Modden and colleagues [24] were unable to demonstrate an effect for two computerized interventions to remediate hemianopsia compared to standard occupational therapy. Although this RCT may have been underpowered, results challenge the previous recommendation and are more consistent with clinical wisdom regarding the irreversibility of visual field loss secondary to stroke.

INSERT TABLE 3 ABOUT HERE

Recommendations**.** There is continued support for the use of visual scanning to improve left visual neglect after right hemisphere stroke as a Practice Standard (Table 3). The inclusion of left hand stimulation or limb activation in visual scanning training should be considered to increase efficacy of rehabilitation for neglect after right hemisphere stroke (Practice Guideline). Based on current evidence, as well as prior research suggesting that functional improvements are associated with compensation, the CRTF does not now recommend the use of computer-based training to extend visual fields.

Rehabilitation of Memory Deficits

The CRTF reviewed 7 Class I studies,[37-43] 7 Class II studies[44-50] and 6 Class III studies[50-56] addressing remediation of memory. Many of these studies focused on specific types of memory impairments rather than global memory functioning. Consequently, the CRTF has organized the more recent studies by the type of memory functioning to be improved. The studies fall into three major categories of functional memory problems 1) prospective remembering; 2) recall of information for the purpose of performing everyday tasks; and 3) memory for routes and navigation. All of the studies utilized a variety of memory strategies previously discussed by the CRTF.

Prospective memory**.** PM is defined as the ability to recall and execute at a future time an intention. There is strong evidence from Class I studies to support assistive technology training as a way to improve the likelihood of future intentions being carried out.[38-41] Lemoncello and colleagues [40] demonstrated the use of a novel assistive technology device which prompts participants with audiovisual reminders at scheduled prospective times on a person's home television screen. Results showed significant advantage of PM prompting compared to a no prompting condition. Two Class I studies [38, 39] suggest that use of a PDA compared with non-electronic memory compensations may lead to fewer functional memory failures and *less use* of internal memory compensations, with no differences in general memory performance. The majority of participants in these studies had sustained a TBI, although several studies also included participants who had sustained a stroke. [39, 40] These results are supported by Class II [50] and Class III [52]evidence demonstrating improved task completion with the use of a PDA.

Shum and colleagues [43] examined compensatory PM training to maximize use of a diary or organizational device for writing reminders, appointments, and note-taking to minimize PM failure, with or without self-awareness training. Training in compensatory strategies was found to increase note-taking independently of self-awareness training. Bergquist and colleagues [37] compared two internet-based interventions on memory performance and use of compensations to carry out meaningful activities in daily life: active calendar acquisition training, compared with use of a diary-only to log day-to-day events. There were no differences on compensation use; the authors suggested that both conditions may have had a therapeutic effect by focusing on recall of future events and historical information. Results of these interventions are notable in light of evidence that the use of external memory compensations (e.g. checking things off on a calendar) is a stronger predictor of activity limitations after TBI than the degree of cognitive impairment [57] and may not require changes in awareness.

One Class I study [42] used visual imagery as the main ingredient in the PM training, based on the idea that visual imagery can strengthen the cue-action association, compared with a control condition of brief education. Individuals with moderate to severe TBI's were trained to make associations between prospective cues and an intended action. Visual imagery training appeared to improve PM functioning by strengthening the "memory trace" and "automatic recall" of intentions. Generalization was demonstrated by participants making fewer PM failures in their daily lives. Two Class II studies [45, 46] investigated self-imagination as a mnemonic strategy to enhance episodic memory, with respect to a PM task. Participants who were trained on a self-imagination technique demonstrated a 66% advantage in prospective remembering, compared with just using rote rehearsal.

Improving memory for everyday tasks. Two Class II studies evaluated group-based memory training techniques to improve recall of information for the purpose of performing everyday tasks, compared with no intervention, after a TBI[49] or single stroke. [44] O'Neill and colleagues [49] used a group training intervention focused on internal memory strategy training and found improvement on everyday memory measures, with greater effect for mild and moderately impaired participants. Miller and colleagues[44] studied the use of a group memory training program patients during the chronic stage of recovery after a single stroke. The intervention included education about memory and the use of both internal/mental strategies and external compensatory aides. Results included significant improvement on measures of delayed recall and assessments of PM, with more marked gains for individuals with higher education or higher measured intelligence. Shorter time post stroke was associated with less improvement of PM.

Memory for routes and navigation. Limited evidence was available to support the use of memory training strategies to improve memory for routes and navigation. One Class II study[48] suggests that the benefits of errorless learning extend to practical route memorization. One Class III study[51] suggests that intensive training in virtual navigational tasks may result in an enhancement of memory function for adults with acquired brain injury.

INSERT TABLE 4 ABOUT HERE

Recommendations. In prior reviews, the CRTF has consistently recommended a Practice Standard of compensatory memory strategy training for mild memory impairments after TBI, including the use of internalized strategies and external compensations. Current evidence supports the use of visual imagery, association techniques, and the use of assistive technology for the treatment of prospective remembering difficulties in persons with mild memory impairment (Practice Standard) (Table 4). These recommendations are consistent with a recent systematic review of neuropsychological rehabilitation for PM deficits. [58] Memory strategy training is also recommended for the improvement of recall in the performance of everyday tasks in people with mild memory impairments after TBI (Practice Standard). Current evidence supports the use of group-based memory strategy training for the purpose of improving PM and recall in the performance of everyday tasks after TBI, and extends this recommendation to the treatment of people with mild to moderate memory impairments after stroke (Practice Option). Current findings are consistent with prior evidence suggesting that internal strategies are more effective for participants with less severe memory impairments and greater cognitive reserve.

In previous reviews, the CRTF focused its recommendations on particular techniques for improving memory function, such as the use of errorless learning techniques and externally-directed assistive devices for patients with moderate to severe memory impairments. Current literature suggests increased emphasis on use of assistive technology and remote treatment delivery using the Internet, but no new evidence to support changing prior recommendations.

Rehabilitation of Communication and Social Cognition

We reviewed 2 Class I [59,60] studies, 1 Class II [61] study, and 5 Class III [62 - 66] studies in the area of communication, predominantly after TBI. One Class III investigation included 5 participants with right-hemisphere CVA. [64]

Remediation for specific language impairments. One Class II study [61]examined the effectiveness of a structured cognitive-based approach to improving reading comprehension compared to a no-strategy control condition, after TBI or stroke. The treatment condition consisted of learning a reading strategy implemented at three different phases in the reading process: pre-reading, during reading, and post-reading. The results indicate that the treatment strategy was associated with greater immediate and delayed recall of information, greater efficiency of delayed recall (as measured by the time taken to recall units of information), and increased accuracy of sentence verification. The authors emphasize the need to match reading comprehension strategies to patient-specific needs and abilities as a more clinically effective approach.

Lundgren and colleagues [64] and Brownell and colleagues [65] provide Class III evidence to support the treatment of metaphor interpretation following right-hemisphere CVA and TBI, respectfully. Lundgren and colleagues [64] examined whether a structured intervention focused on improving use of semantic associations could improve oral interpretations of metaphors in 5 participants with right hemisphere CVA. Significant improvement on oral metaphor interpretation was noted though little improvement was demonstrated on an untrained line orientation task. In the second investigation, Brownell and colleagues [65] investigated the effectiveness of the same metaphor interpretation task with a group of 8 subjects 3-20 years following moderate to severe TBI. Six of the 8 participants demonstrated significant improvements in oral metaphor interpretation with 3 out of the 6 demonstrating maintenance effects at 3-4-month follow-up.

Specific treatments for remediation of emotional perception deficits. Two Class I studies [59, 60] and 1 Class III study [66] provide support for the remediation of emotional perception deficits following ABI. McDonald and colleagues [60] randomized 20 participants to either an intervention group or a wait-list group. Treatment involved a manualized program to improve the ability to perceive and distinguish between prosodic emotional cues. Group differences in test performance favored the treatment group; however, only 6 of the subjects allocated to the treatment group demonstrated measurable improvements on test scores. None of the participants demonstrated a treatment effect at one-month follow-up.

Neumann and colleagues [59] randomized a group of 71 participants with TBI to either one of two treatment groups or a cognitive-training control group. All treatments were provided through one-on-one computer-assisted interventions facilitated by a therapist The first treatment taught participants to recognize emotions from facial expressions (Faces). The second treatment taught participants to infer emotions from contextual cues presented in a story format (Stories). Participants in the control condition played a variety of online, publicly available computer games that targeted cognitive skills but did not provide any type of emotion-related training. On tests of facial emotion recognition, there was a significant main effect reported between the Faces group and the control group, but not between the Stories group and the control group. There were no significant main or interaction effects between Faces, Stories and control conditions on the ability to infer emotions from stories, and no generalization to measures of empathy or neuropsychiatric behaviors. These findings replicate a previous Class III investigation. [66] The authors indicate that facial emotion recognition training is effective for individuals with TBI and that benefits of treatment can be maintained up to 6 months following intervention. However, they indicate that the training failed to show a generalization effect to emotion perception based on contextual cues. The authors suggest that group treatment may provide an opportunity to practice emotion recognition in a functional setting and subsequently promote generalization of performance.

Group treatment for social communication deficits. Braden and colleagues [63] conducted a Class III feasibility investigation with pre-post and six-month follow-up assessments to determine the effectiveness of a group interactive structured treatment approach combined with individual treatments for improving social skills following TBI. This study extends the findings of a previous RCT study by the same researchers [67] to 30 participants with post-acute TBI with identified social communication deficits plus a history of psychiatric/psychological disorder or substance abuse or those with additional neurological complications, such as stroke, hypoxia, multiple sclerosis or others (TBI-Plus). Results demonstrated that, following a 13-week group social communication skills intervention, the TBI-plus participants made statistically significant gains on subjective social communication skills and quality of life measures, which were maintained at 6-month follow-up. Additional Class III [62] evidence provides support for the effectiveness of group treatment for remediation of social communication deficits following TBI.

INSERT TABLE 5 ABOUT HERE

Recommendations. The CRTF previously recommended cognitive interventions for specific language impairments such as reading comprehension and language formulation after left hemisphere stroke or TBI (*Practice Guideline*). A well-designed Class II study [61] provides additional evidence to support this recommendation (Table 5).

The CRTF previously recommended as a *Practice Standard* specific interventions for functional communication deficits, including pragmatic conversational skills following TBI. Two Class III studies reporting the effectiveness of metaphor interpretation training following right hemisphere stroke [64] and TBI [65] provide support for this recommendation. One Class I [59] and one Class III study [66] suggest that specific intervention to improve the recognition of emotions from facial expressions may be effectively incorporated as component of the *Practice Standard* for treating functional communication deficits after TBI (Table 5). However, the CRTF notes that this effect may be specific to this training and does not generalize to training emotional perception based on prosodic or semantic-contextual cues, nor to empathy or neuropsychiatric behaviors.

Two Class III studies [62, 63] support the recommendation (*Practice Option*) for group-based interventions for the remediation of language deficits after left hemisphere stroke and for social-communication deficits after TBI.

Rehabilitation of Executive Functioning

The CRTF reviewed 15 Class I [68-82] or Class Ia [83-85] studies, 3 Class II [86-88] studies, and 19 Class III [89–107] studies of interventions for executive functioning. The central aspect of most of these interventions is the facilitation of *metacognitive knowledge* (awareness) and metacognitive self-regulation (e.g., goal setting, planning, initiation, execution, self-monitoring, and error management). Many of these interventions addressed multiple aspects of executive dysfunction within an integrated treatment approach.

Goal Management Training. We reviewed 2 Class I studies,[69, 70] 1 Class II study,[86] and 1 Class III study [93] addressing the remediation of executive functioning using GMT.

A Class I study [69] investigated the effectiveness of GMT compared to BHW control group in a mixed population. GMT produced significant benefits on sustained attention and behavioral regulation, while no differences were seen in the BHW group for any of the tasks. Unfortunately, neither group demonstrated significant improvements on self-reported problems in everyday functioning. However, a Class II study[86] showed GMT to be effective in improving the skills needed for every day financial management on participants' self-selected functional goals that were a focus of treatment.

Novakovic-Agopian and colleagues conducted a Class I study[70] to determine the feasibility of an intervention directed at "goal-oriented attentional self-regulation skills" with individuals with chronic brain injury and mild to moderate difficulties in executive functioning. The group-based intervention focused on attention regulation (including mindfulness exercises) and use of a metacognitive strategy ("stop-relax-refocus") as well as the application of training to individual goals. The executive intervention was compared with didactic brain injury education. Participants exhibited a decrease in task failures on a complex functional task following goal-oriented attention training, related to protection of working memory from distractions. These gains were maintained at 5-week follow-up. A subset of participants was administered functional MRI during a visual selective attention task, pre and post treatment, to examine changes in neural processing.[108] Modulation of neural processing in extrastriate cortex was enhanced by attention training. Neural changes in prefrontal cortex, a proposed mediator for attention regulation, were inversely related to baseline state. These results suggested that enhanced modulatory control over visual processing and a rebalancing of prefrontal functioning may underlie improvements in attention and executive control. A subsequent modularity analysis[109] demonstrated that the modularity of brain network organization at baseline predicted improvement in attention and executive function after cognitive training, with higher baseline modularity related to greater adaptation in response to goal training.

A systematic review of GMT noted that for most studies that demonstrated effectiveness of GMT, it was part of an intervention that incorporated PST focused on personal goals, and included application of GMT to daily life tasks.[110]

The CRTF reviewed additional Class I [68] and Class Ia [83] studies that reflect these treatment components. Spikman and colleagues [68] conducted a multicenter study to evaluate the effects of treatment for dysexecutive problems on daily life functioning after acquired brain injury. The multi-faceted intervention incorporated aspects of GMT[69] and PST[111] in a general planning approach in three stages (information and awareness; goal setting and planning; initiation, execution and regulation). The experimental intervention was compared with an individually administered, computerized cognitive training package consisting of several repetitive cognitive tasks aimed at improvement of general cognitive functioning, with no therapist-directed strategic approaches to the tasks. Improvements in executive functions and resumption of social roles (based on structured interview) were observed after both treatments; participants in the multi-faceted treatment demonstrated larger benefits, and maintained gains, in their ability to set and accomplish real-life goals, regulate a series of real-life tasks, and resume effective social roles. The reliance on therapists' ratings and lack of blind outcome assessments limits the interpretation of these results. Cantor and colleagues[83] also evaluated a multi-faceted intervention that incorporated metacognitive skills that could be applied across a range of real-life activities through PST, attention training, and emotional regulation. In comparison with a wait-list control group, the experimental intervention produced significant benefits on self-reported executive functioning and problem solving, but not on other measures of neuropsychological functioning, attention, awareness, self-efficacy, emotional regulation, participation or quality of life.

Metacognitive strategy training. One Class I,[81] 1 Class II [85] and 3 Class III studies [89, 90, 92] addressed the remediation of executive functioning using specific aspects of metacognitive strategy training. The Class III single-case studies evaluated the effectiveness of metacognitive strategy training for improving on-line awareness and self-management of errors during functional activities. [89, 90, 92] For example, Ownsworth and colleagues[90] examined the use of MST to improve performance on a cooking task through therapist-guided evaluation and feedback using the "pause, prompt, praise" technique.[112] Individuals receiving MST demonstrated a significant reduction in error frequency, a significant decrease in therapist checks, and a significant increase in self-corrected errors on the cooking task; participants who only received behavioral practice demonstrated no difference in self-corrected errors and greater reliance on therapist checks.

A Class I study by Schmidt and colleagues[81] also utilized the "pause, prompt, praise" technique during a meal preparation task to investigate the effects of video-and-verbal feedback, verbal feedback alone, or experiential feedback on error management in participants with TBI with impaired self-awareness. Participants were typically seen during postacute rehabilitation, several years after sustaining moderate to severe TBI, and exhibited deficits in intellectual and emergent (online) awareness. Participants in the video-and-verbal feedback group showed significantly improved online awareness, measured by the number of errors during task completion, than either of the comparison interventions. Further, the video-and-verbal feedback group demonstrated greater intellectual awareness after treatment, with no increase in emotional distress or changes in their perceptions of recovery or rehabilitation.

Cognitive Orientation to Occupational Performance. A number of the studies cited above were directed at the application of MST to functional task performance. [81, 86, 90] Along this line, there was a notable emergence of research on the effectiveness of an approach integrating functional skills training and metacognitive strategy training through CO-OP. This procedure includes client centered goal setting, particularly in relation to performance of functional activities, and the use of a global metacognitive strategy of Goal-Plan-Do-Review. The remediation of specific cognitive components or impairments is avoided in favor of interventions directly at the level of relevant client-centered functional activities.

We reviewed 11 studies investigating the effectiveness of CO-OP after TBI or stroke, involving 3 Class I [71-73], 1 Class Ia [84] studies, 1 Class II [87], and 6 Class III [94-99] studies.

Dawson and colleagues adapted an occupation-based strategy training based on the CO-OP for patients with executive dysfunction after TBI.[84, 94] A Class Ia pilot RCT was conducted for patients with chronic TBI, all of whom were at least 1-year post injury and an average of 10 years post injury.[84] The experimental intervention included the identification of meaningful problems in each participant's everyday life, translated into functional goals (e.g., keep papers organized; schedule activities to avoid fatigue), and application of guided discovery and the metacognitive problem-solving strategy to the goals being trained. Participants who received the intervention demonstrated improved performance and satisfaction on trained goals compared with the comparison group. In addition, the intervention resulted in improvement on untrained goals, suggesting near transfer of training, as well as participants reporting increased levels of participation, suggesting generalization of the training to participants daily functioning.

Two Class I studies[71, 72] evaluated the CO-OP intervention compared with SOT to improve performance on functional goals and transfer to untrained activities for people living in the community after a single stroke. Participants were either less than three months post-stroke [72] or more than six months post-stroke.[71] Participants in both conditions chose their own treatment goals; however, in the SOT condition treatment plans were completely therapist driven with an emphasis on impairment-based training whereas in CO-OP therapists helped participants create their own performance plans (guided discovery), taught participants a global metacognitive strategy (goal-plan-do-review) to create and evaluate those plans, and focused entirely on activity-level interventions. In both studies, significant benefits of CO-OP over SOT were apparent on participant and therapist ratings of performance of self-selected activities, as well as greater transfer to untrained activities. An additional Class I study[73] compared CO-OP with an attention control condition (reflective listening) among patients after acute stroke who were receiving inpatient rehabilitation. Participants who received CO-OP showed significant improvements on executive cognitive measures as well as reduced disability in activities of daily living (FIM Scores) at 3 and 6 months after admission, with increasing differences between groups over the 6-month study period.

These studies suggest that a combination of functional skills training at the activity level, and incorporation of metacognitive strategies is related to improved performance on trained tasks, and greater transfer of training to untrained tasks, although the specific effective ingredients of the CO-OP procedure have not been isolated. Rotenberg-Shpigelman and colleagues[82] conducted a Class I study of NFT that incorporated errorless learning (as opposed to trial-and-error learning or error management training) and repeated practice and "overlearning" of task performance. This approach is consistent with the evidence that even people with severe memory and executive impairments can be trained on new routines using errorless learning [55] and that, once learned, these routines can be carried out in novel contexts. The NFT approach places little demands on the cognitive, emotional and physical resources of participants with severe neurologic disabilities, in contrast to the cognitively-demanding use of metacognitive strategies inherent in the CO-OP intervention. A sample of community dwelling chronic stroke survivors attending day rehabilitation (at least one-year post-stroke) received either NFT or treatment as usual (a combination of traditional outpatient therapies). Participants who received NFT showed greater improvements on trained tasks, while neither condition demonstrated improvements on untrained tasks, an outcome that was expected to occur in accordance with the principles of NFT. The investigators suggested that NFT may have more specific effects than CO-OP and be less limited in its applicability to patients with more severe cognitive impairment.

These studies also suggest that the effects of intervention on untrained functional tasks requires the incorporation of deliberate efforts to promote transfer and generalization, including the use of a general metacognitive strategy for planning, implementing and self-monitoring performance of functional activities.

Reasoning, problem solving, and executive regulation of attention. One Class I study [74] examined a top-down strategy (remembering general concepts without emphasizing details) to improve gist-reasoning in participants with chronic TBI. The intervention group improved on gist-reasoning, executive control and verbal working memory, and endorsed significant functional changes in community functioning 6 months-post training., Fong and Howie [85] evaluated an intervention combining multiple components of problems solving, compared with a conventional treatment (including repetitive practice of functional skills or cognitive tasks). The problem-solving intervention produced marginal benefits on paper-and-pencil reasoning tasks but these benefits did not transfer to real-life situations.

Several Class I [76, 77] and Class III [101] studies have examined the effects of treatment on participants with acquired brain injury ability to manage multiple, simultaneous task demands as an aspect of executive functioning. These studies demonstrated highly specific effects on performing trained dual tasks (particularly simultaneous cognitive and motor tasks), with little generalization to broader executive abilities or everyday functioning. An additional Class I study noted above [20] failed to show a benefit of divided attention training on visuospatial treatment for neglect.

Computer-assisted treatment. The CRTF reviewed three Class I [78-80] studies and 1 Class III study [100] addressing computer-based cognitive rehabilitation of executive functioning, including the use of virtual reality (VR) environments. One study reported benefits of computer-based cognitive exercises when combined with standard inpatient stroke rehabilitation.[78] Spikman and colleagues found similar effects of computer-based treatment with metacognitive strategy training on discrete measures of executive functioning.[68] The use of VR was more effective than psychoeducation in enhancing problem solving skills[79] but not significantly better than SOT in improving everyday executive function performance.[80] The use of VR represents a potentially fruitful area for further study. [78-80, 100] At present, there is insufficient evidence to support a recommendation for computer-based cognitive rehabilitation specifically for deficits in executive functioning.

Emotional regulation. There is increasing recognition of the association between metacognitive and emotional regulation, including a specific relationship of alexithymia (difficulty identifying emotions) and multiple aspects of executive functioning. [113-115] Spikman and colleagues [116] conducted a secondary analysis of their RCT for dysexecutive problems[68] to examine patient characteristics related to treatment outcomes. Pre-treatment emotion recognition performance predicted post-treatment resumption of roles and everyday executive functioning. In addition, worse pre-treatment emotion recognition skills negatively affected treatment-induced learning of compensatory strategies for executive dysfunction, whereas pre-treatment dysexecutive deficits did not. These findings suggest that deficits in emotional regulation may play a critical role in patients' ability to apply a strategy for the planning and regulation of complex tasks, and may require specific interventions. [59,60]

Although treatment for difficulties in emotional regulation has been incorporated into some multi-faceted interventions for executive dysfunction [68, 70, 83, 117-119] this requires additional research. Several Class III studies [103-105] evaluated group-based interventions for emotional regulation, specifically directed at self-management of anger and aggression. The interventions included techniques to increase awareness of emotion, manage the expression of anger, problem solving and cognitive restructuring. Treatment effects were limited to the experience and control of anger and aggressiveness with no effect on other aspects of behavioral regulation or emotional symptoms.

A systematic review suggested some benefit of external compensations for milder forms of apathy (diminished initiation, sustained activity and goal-directed behavior) after traumatic brain injury.[120] A single-case study incorporating external compensation and motivational interviewing demonstrated a strong and specific effect on sustained activity and subjective apathy.[102]

INSERT TABLE 6 ABOUT HERE

Recommendations. The CRTF has previously recommended MST (self-monitoring and self-regulation) as a Practice Standard for treating deficits in executive functioning after TBI, including impairments of emotional self-regulation, and as a component of interventions for deficits in attention, neglect, and memory. Current evidence suggests that the incorporation of formal protocols for PST and GMT, and their application to everyday situations and functional activities, should be considered as components of MST during post-acute rehabilitation after TBI

(Table 6). [68-70, 83, 85, 86] Emerging Class I evidence[71-73, 84] supports the incorporation of MST into occupation-based treatment for practical goals and functional skills to promote both acquisition and transfer of functional skills during post-acute rehabilitation after TBI and stroke. Additional Class I evidence [81] suggests that explicit (verbal-and-video) performance feedback should be considered to facilitate the positive effects of metacognitive strategy training (Practice Guideline) (Table 6).

Indirect evidence from Class I studies[70, 83] supports the existing Practice Option indicating that group-based interventions may be considered for remediation of executive and problem solving deficits after TBI.

For patients with severe cognitive (executive) deficits, including limitations of emergent awareness and use of compensatory strategies, the use of direct, skill-specific training including errorless learning may be considered to promote performance of specifically trained functional tasks, with no expectation of transfer to untrained activities.[82] While the direct evidence for NFT is limited to participants with chronic stroke, the CRTF considered that there is a sound clinical rationale and indirect evidence for applying this recommendation to the treatment of people with severe cognitive impairments after TBI (Practice Option). There is preliminary evidence suggesting that MST as a component of training on functional activities may increase the effectiveness of acute rehabilitation for patients with cognitive impairment after stroke (Practice Option) (Table 6).

Comprehensive Rehabilitation Programs

In our initial review we included a discussion of both multi-modal interventions and comprehensive-holistic programs. In the current review, all of the multi-modal interventions were computerized, which is a noteworthy shift in current treatment trends. Modular approaches to cognitive remediation are typically aimed at a single cognitive impairment; patients with multiple impairments may receive a mix of modular treatments that target several cognitive impairments. [121] Comprehensive-holistic programs typically target specific cognitive impairments but also provide individual and group therapies that address self-awareness of the impact of cognitive deficits, interpersonal and emotional functioning, and psychological coping through an organized and integrated therapeutic environment. [121] The CRTF reviewed 5 Class I [122-126], 2 Class II and 20 Class III [129-148] studies of comprehensive rehabilitation through either multi-modal or comprehensive-holistic programs.

Multi-modal, computer-based interventions. In this section we include discussion of 3 Class I [122-126] and 4 Class III [145-148] studies of multi-modal computer-based programs for the remediation of cognitive skills. Some utilized computer-based retraining packages that are meant to be administered or directed by a rehabilitation professional. [124, 126, 146] Others utilized commercially available computer-based brain training programs that patients could potentially initiate or direct with little, if any, therapist involvement.[145, 147, 148]

Two of the most encouraging and rigorous studies utilized the RehaCom Software package. Lin and colleagues [126] conducted a Class I study that demonstrated not only the effectiveness of computerized cognitive rehabilitation for deficits in memory and executive functioning, but also the changes in cerebral functional connectivity that may underlie post-training improvements during the post-acute period of recovery (6-10 months after a first stroke). Participants were randomized to receive 60 hours of computerized cognitive retraining with

RehaCom or no treatment. Treatment recipients showed improvements in attention, memory and increased functional connectivity of the hippocampus with frontal and parietal cortical areas, while the control group demonstrated decreased hippocampal-cortical connectivity. Moreover, improvements in neuropsychological performance correlated with increased functional connectivity. This finding is supported by a Class III study[146] demonstrating improvements in attention/working memory and new learning and memory after treatment through RehaCom. An additional Class I study[124] demonstrated benefits on cognitive and daily functioning from broadly defined, therapist-directed computer-based treatments as an adjunct to “standard neurorehabilitation” for participants with TBI or stroke during post-acute recovery. It is notable that the RehaCom package incorporates components that have contributed to the efficacy of other rehabilitation techniques, including: repeated stimulation, intensity of training, adjusting task difficulty to the patient’s performance, feedback, therapist involvement, and simulated functional tasks.

***Comprehensive-Holistic Neuropsychological Programs*.** The CRTF reviewed 2 Class I[122, 123], 2 Class II[127, 128] and 16 Class III [129-144] studies of comprehensive-holistic rehabilitation. A pilot RCT investigated CogSMART, a didactic approach toward development of compensatory strategies for management of PCS, PM, attention and vigilance, learning and memory, and problem solving.[122] This investigation was conducted with Veterans with chronic PCS an average of 4 to 5 years after primarily mild TBIs. All participants were seeking employment and received one year of SE. For the first 3 months, some participants were randomly assigned to receive CogSMART for 1 hour per week in addition to the 2 SE weekly visits; the control group received enhanced SE of 2 additional visits per week to control for nonspecific effects. CogSMART was effective in reducing PCS and improving PM at the end of treatment,[122] and these benefits were maintained at completion of the 12 month SE program.[149] Improvement in PCS was seen primarily in affective symptoms, to less extent in cognitive symptoms, with no effect on somatic symptoms. CogSMART participants also reported greater subjective quality of life after SE although there were no differences between conditions on competitive work attainment. Co-morbid PTSD was evident in 74 percent of Veterans in this study. Veterans with greater PTSD and depression severity reported greater PCS at all assessment points, however CogSMART-related improvements in PCS did not vary as a result of psychiatric symptomatology.[150] Results from these studies are consistent with an earlier Class I study[151] and suggest that psychoeducation and strategy training [122,133,149, 150] may be an effective adjunct or stand-alone program for reducing PCS after mild TBI. In addition, the presence of co-morbid PTSD or depressive symptoms should not preclude participation in cognitive rehabilitation interventions in this population.[150]

Current findings from 1 Class II[128] and 2 Class III[138,139] studies support and extend existing evidence showing that individualized comprehensive multidisciplinary neurorehabilitation programs may lead to significantly improved short and long term functional, cognitive and psychosocial outcomes in the areas of independent living, societal participation (including occupational functioning), and self-reports of emotional well-being and quality of life. Findings from several Class III studies suggest these programs may also lead to reduced caregiver burden (both in terms of emotional burden and psychological health)[129] and a significant reduction of societal costs.[130] These findings apply to in individuals with both traumatic and non-traumatic brain injuries, regardless of severity or time post injury.[139-141] However, findings from several Class III studies suggests starting rehabilitation earlier post injury is associated with greater improvements in mood, cognitive functioning, quality of life [138,142] and better functional outcomes[140, 141] than treatment that begins late post-injury.

The Class II study by Vestri and colleagues[127] compared patients with acquired brain injury, primarily TBI and stroke, who received either multidisciplinary individual treatments only or combined individual and group treatments, Participants in both conditions improved, with less functional impairment after treatment for those receiving combined individual and group interventions. Additional Class III evidence [91]indicates that structured group treatment, within an outpatient rehabilitation setting, improves self-awareness and the effective use of metacognitive strategies for people one or more years after an acquired brain injury. These results are consistent with existing evidence that group intervention improves psychological well-being following acquired brain injury[67,117,152] Evidence from several Class III studies suggests that rehabilitation programs incorporating goal directed treatments with an emphasis on individualized client centered goal setting may significantly improve goal attainment [131,132,135] and translate to greater levels of residential independence and occupational functioning.[135, 136]

INSERT TABLE 7 ABOUT HERE

Recommendations. The current evidence is consistent with our existing recommendation that post-acute, comprehensive-holistic neuropsychological rehabilitation should be provided to reduce functional, cognitive and psychosocial disability after TBI (Practice Standard). Whereas the previous research focused on individuals with TBI, the present results support extending the recommendation to individuals with both traumatic and non-traumatic brain injuries, regardless of severity or time post injury. [128,138-141] Comprehensive neuropsychological programs should integrate individualized interventions to address cognitive and interpersonal functioning after acquired brain injury. Such interventions should be goal directed and emphasize individualized client centered goal setting to promote enhanced residential independence and occupational functioning[135,136] (Practice Option) (Table 7). Group interventions may be considered as part of comprehensive-holistic neuropsychological rehabilitation to address the functional application of specific interventions and improve psychological well-being[67, 91, 117, 127, 152] (Practice Option). While not a formal recommendation, the CRTF recognizes that the presence of PCS and co-morbid psychiatric symptomatology should not preclude participation in cognitive rehabilitation that includes psychoeducational and cognitive strategy training after mild to moderate TBI. [122,150]

Based on 2 Class I [124,126] and one Class III[146] study, multi-modal, computer-assisted cognitive retraining with the active involvement and direction of a rehabilitation therapist is recommended as a component of neurorehabilitation for the remediation of attention, memory, and executive function deficits following stroke or TBI. Computer-assisted cognitive retraining programs should stimulate the cognitive domains of interest, adapt task difficulty to the patient's level of performance, and provide feedback and objective performance data (Practice Guideline) (Table 7).

DISCUSSION

Together with our prior reviews, the CRTF has now evaluated 491 interventions (109 Class I or Ia, 68 Class II, and 314 Class III) that address the effectiveness of cognitive rehabilitation after TBI or stroke. Based on these cumulative reviews, the CRTF makes 29 recommendations for evidence-based, clinical practice of cognitive rehabilitation (9 Practice Standards, 9 Practice Guidelines and 11 Practice Options). Several trends are apparent in the current review of the literature, which are reflected in the current recommendations. There is a trend toward increased specificity of interventions within the broad domains of functioning, which is consistent with efforts to specify the active ingredients of rehabilitation treatments.[153] For example, several studies examined treatment of working memory[7,8] or specific aspects of working memory,[15,16] within the broader domain of rehabilitation for attention. Several new recommendations are made based on specific aspects of metacognitive strategy training such as prompting for error recognition[90] and providing specific forms of feedback[81] as active components of occupational therapy interventions, and specific training in facial emotion recognition as an active component of pragmatic communication treatment.[59]

There is a trend toward the incorporation of interventions for emotional regulation within cognitive rehabilitation.[59,68,83,116] This is consistent with a central tenet of holistic neuropsychological rehabilitation[117,154] as well as increased recognition of the interaction of cognitive and emotional regulation as an integral aspect of cerebral organization.[155] While difficulties with emotional regulation may mediate the effectiveness of cognitive rehabilitation,[116] psychiatric co-morbidities may not.[63,150, 154]

Computer-based cognitive interventions represent a larger number of studies in the current review than in prior reviews, directed at both specific cognitive impairments as well as incorporating interventions across multiple cognitive domains. Computer-based cognitive training can improve traditional rehabilitation of cognitive functions by enhancing the consistency and precision through more immediate feedback, systematized delivery, and difficulty level adjustments. The continuous, adaptive adjustment of task difficulty based on a patient’s performance is critical for promoting neuroplasticity.[157] The use of tasks with equivalent content that do not include adaptive adjustment of task difficulty produce less improvement and transfer of cognitive functioning.[158-161] Computer-based cognitive interventions also have the potential to bridge some common gaps in treatment access for individuals with brain injury, including restrictions imposed by disability-related limitations, geographical barriers, funding restrictions, and time constraints of complex contemporary lifestyle. [162,163] Unfortunately, proper scientific examination and evidence of efficacy has traditionally lagged behind the rapid expansion of computerized brain training programs with claims to change brain structure and function. [164-166] The CRTF found evidence that computer-based direct attention training for modular impairments in working memory can improve specific cognitive functions and generalize to improved subjective complaints. [7, 18] The use of direct attention training for specific "modular" impairments in working memory, including the use of computer-based interventions, as a component of post-acute rehabilitation of individuals with acquired brain injury has therefore been upgraded to a Practice Guideline. The current Practice Standard continues to emphasize that treatment of attention deficits should incorporate both direct attention training and metacognitive strategy training, to increase task performance and promote generalization to daily functioning after TBI or stroke during the post-acute stages of recovery. New evidence on multi-modal computerized training of attention, memory, and executive functions indicates that this type of intervention is effective (Practice Guideline) for individuals with stroke and TBI when managed by a rehabilitation clinician and when the program adheres to the principles of neuroplasticity (direct stimulation of a cognitive domain, ongoing adaptive adjustment of task difficulty, and immediate objective feedback on task performance).[157]

There continues to be evidence to support the use of group-based interventions across cognitive domains, although the direct evidence to distinguish the specific effects or comparative effectiveness of group-based and individual interventions remains limited. [127,152] The existing evidence suggests that a combination of individual and group-based treatment may increase effectiveness. Group-based interventions appear to provide increased contextualization and support for social interaction, psychological adaptation and maintenance of goals. [67, 91, 144] Our current review found sufficient evidence for group interventions that target impairments of memory, language and social communication deficits, as well as for increasing awareness,[91] goal management [70, 136] and emotional regulation [68] aspects of executive functions. With respect to memory, like the studies on individual cognitive rehabilitation, the evidence on group interventions also suggests that internal memory strategies are more effective in people with either TBI or stroke who have mild to moderate impairment of memory.[44] Improvement in goal management was demonstrated not only on performance of a complex functional task, but also on fMRI following group treatment incorporating regulation of attention through mindfulness training and metacognitive strategies.[70,108, 109] These new findings provided the basis for a Practice Option for group treatment for aspects executive function impairment following TBI. More generally, the CRTF recognizes that group interventions provide the opportunity for the person to interact with others with similar deficits, [91, 144] which may be therapeutic in ways beyond just cognitive functioning, as suggested by the research on the efficacy and effectiveness of holistic comprehensive neuropsychological rehabilitation programs. [83,117]

Evidence regarding patient characteristics that influence treatment effectiveness remains limited. Compared to prior reviews, the current review includes a greater percentage of studies assessing stroke and mixed acquired brain injury populations. As such, there are several instances in which prior recommendations have now been extended for utilization for people who sustained a stroke. In terms of time post injury, this and previous reviews include studies spanning the full spectrum of recovery from acute to chronic populations, and has found evidence that cognitive rehabilitation can lead to clinically significant improvements even years after the initial injury.[117, 140,141, 144] As noted above, cognitive rehabilitation can be effective for people with physical and psychological co-morbidities in addition to TBI. [63,150, 154] Finally, this review provides evidence that various cognitive rehabilitation interventions can be effectively tailored to individuals across levels of injury severity and across levels of neurocognitive impairment. [55, 56, 82]

The bulk of studies included in this review compare the effectiveness of cognitive rehabilitation interventions to either no treatment or standard treatment alone. While this helps elucidate the utility of cognitive rehabilitation and offers treatment recommendations based on observed cognitive impairments, it does not speak to the specific patient characteristics or modes of treatment delivery that likely play a role in mediating intervention success. Further, it does not allow for a comparative assessment of different cognitive interventions across and within patient impairment profiles. The CRTF recommends that future research be directed towards identifying those specific patient characteristics (i.e., psychological insight; residual cognitive reserve; psychiatric comorbidity) and treatment delivery variables (i.e., frequency and intensity) that might influence one's response to particular treatments.

Limitations

There are several significant limitations to the current systematic review. The review covers only the literature published (print or electronic) through 2014 and identified by December 15, 2015. This results in a significant gap in the published literature that may inform our clinical recommendations. This largely reflects the time and labor required by members of the CRTF, and our attempts to maintain an acceptable level of rigor and quality to recommendations. It is our hope that readers of these reviews will adopt a similar process of clinical and scientific inquiry to examine the current literature. Second, different methodologies for conducting systematic reviews have occurred since our initial publication almost 20 years ago. However, the CRTF has elected to use our extant procedures in order to maintain the consistency of methods and recommendations among our reviews. More specifically, despite our attempts to maintain a level of rigor, we did not include any formal assessment of risk of bias in our evaluation of studies for this review. We recognize that the failure to include formal assessment of study quality in this systematic review may influence the precision, applicability and confidence in our results and recommendations. [167] It is worth noting that a prior review addressing methodological study quality [4], including the formal assessment of risk of bias, supported the clinical recommendations from our prior systematic reviews. [1 - 3]

Conclusions

In our initial review, we concluded that "cognitive rehabilitation should always be directed toward improving everyday functioning, and should include active attempts to promote generalization or directly apply compensatory strategies to functional contexts." Evaluation of rehabilitation effectiveness typically occurs at the impairment level, with the expectation that this will translate into changes in daily functioning. However, this expectation is a limiting factor in evaluation of rehabilitation effectiveness. For example, the IOM report on cognitive rehabilitation therapy for TBI[121] noted that "*there is evidence from controlled trials that internal memory strategies are useful for improving recall on decontextualized, standard tests of memory, [but] there is limited evidence that these benefits translate into meaningful changes in patients' everyday memory either for specific tasks/activities or for avoiding memory failures. Therefore, an increased emphasis on functional patient-centered outcomes would allow for a more meaningful translation from cognitive domain to patient functioning*" (pg. 13). This will require ongoing development of interventions and outcome measures that address the application of cognitive abilities to performance of activities in everyday functioning. The use of subjective patient-reported outcomes should provide a direct measure of "meaningful changes" in patients everyday functioning, including symptoms, functional status, and health-related quality of life.[168] Unfortunately, reliance on subjective outcomes is typically "downgraded" from a methodological perspective on the basis of risk of "bias" and threats to external validity. This is an issue that extends beyond cognitive rehabilitation to the nature and measurement of meaningful rehabilitation outcomes, and the question of which outcomes we (and the patients we serve) value. Outcomes should also be "meaningful" in relation to the designated targets of an intervention, presumed mechanisms of change, and anticipated effects of the intervention.[153] For example, research that is intended to demonstrate that a cognitive intervention promotes neuroplasticity will necessarily assess changes in functional cerebral connectivity (for example), but should not be required to demonstrate changes at the participation level as an indication of a valid treatment effect. In clinical practice, it is the responsibility of the clinician to make overt the targets of the intervention and to make sure that any evidence-based intervention is relevant to the person's everyday functioning. We believe that the current review and recommendations continue to move the field forward and will contribute toward the evidence-based practice of cognitive rehabilitation.

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Table 1. Definition of Levels of Recommendations

Practice Standards:	Based on at least one, well-designed Class I study with an adequate sample, with support from Class II or Class III evidence, that directly addresses the effectiveness of the treatment in question, providing substantive evidence of effectiveness to support a recommendation that the treatment be specifically considered for people with acquired neurocognitive impairments and disability.
Practice Guidelines:	Based on one or more Class I studies with methodological limitations, or well-designed Class II studies with adequate samples, that directly address the effectiveness of the treatment in question, providing evidence of probable effectiveness to support a recommendation that the treatment be specifically considered for people with acquired neurocognitive impairments and disability.
Practice Options:	Based upon Class II or Class III studies, , that

directly address the effectiveness of the treatment in question, providing evidence of possible effectiveness to support a recommendation that the treatment be specifically considered for people with acquired neurocognitive impairments and disability.

Table 2: Recommendations for treatment of attention deficits

Intervention	*Level of Recommendation*
Treatment of attention deficits should incorporate both direct attention training and metacognitive strategy training to increase task performance and promote generalization to daily functioning after TBI or stroke during the post-acute stages of recovery.	Practice Standard
Direct attention training for specific “modular” impairments in working memory, including the use of computer-based interventions, should be considered to enhance both cognitive and functional outcomes during post-acute rehabilitation for acquired brain injury.	Practice Guideline

Table 3: Recommendations for treatment of visuoperceptual deficits

Intervention	*Level of Recommendation*
Visuospatial rehabilitation that includes visual scanning training is recommended for left visual neglect after right hemisphere stroke	Practice Standard
The use of isolated microcomputer exercises to treat left neglect after stroke does not appear effective and is not recommended	Practice Guideline
Left hand stimulation or forced limb activation may be combined with visual scanning training to increase the efficacy of treatment for neglect after right hemisphere stroke	Practice Guideline
Electronic technologies for visual scanning training may be included in the treatment of neglect after right hemisphere stroke	Practice Option
Systematic training of visuospatial deficits and visual organization skills may be considered for persons with visual perceptual deficits, without visual neglect, after right hemisphere stroke as part of acute rehabilitation	Practice Option
Specific gestural or strategy training is recommended for apraxia during acute rehabilitation for left hemisphere stroke	Practice Standard

Table 4: Recommendations for treatment of memory deficits

Intervention	*Level of Recommendation*
Memory strategy training if recommended for the improvement of prospective memory in people with mild memory impairments after TBI or stroke, including the use of internalized strategies (e.g., visual imagery, association techniques) and external memory compensations (e.g. notebooks, electronic technologies)	Practice Standard
Memory strategy training if recommended for the improvement of recall in the performance of everyday tasks in people with mild memory impairments after TBI, including the use of internalized strategies (e.g., visual imagery, association techniques) and external memory compensations (e.g. notebooks)	Practice Standard
Use of external compensations with direct application to functional activities is recommended for people with severe memory deficits after TBI or stroke.	Practice Guideline
For people with severe memory impairments after TBI, errorless learning techniques may be effective for learning specific skills or knowledge, with limited transfer to novel tasks or reduction in overall functional memory problems.	Practice Option
Group-based interventions may be considered for remediation of mild to memory deficits after TBI or stroke, including the improvement of prospective memory and recall of information used	Practice Option

in the performance of everyday tasks.	

Table 5: Recommendations for Remediation of Communication and Social Cognition

Intervention	*Level of Recommendation*
Cognitive-linguistic therapies are recommended during acute and post-acute rehabilitation for language deficits secondary to left hemisphere stroke.	Practice Standard
Specific interventions for functional communication deficits, including pragmatic conversational skills and recognition of emotions from facial expressions, are recommended for social communication skills after TBI.	Practice Standard
Cognitive interventions for specific language impairments such as reading comprehension and language formulation are recommended after left hemisphere stroke or TBI.	Practice Guideline
Treatment intensity should be considered a key factor in the rehabilitation of language skills after left hemisphere stroke.	Practice Guideline
Group based interventions may be considered for remediation of language deficits after left hemisphere stroke and for social-communication deficits after TBI.	Practice Option
Computer-based interventions as an adjunct to clinician-guided treatment may be considered in the remediation of cognitive-linguistic deficits after left hemisphere stroke or TBI. Sole reliance on repeated exposure and practice on computer-based tasks without some involvement and intervention by a therapist is not recommended.	Practice Option

Table 6: Recommendations for treatment of executive function deficits

Intervention	*Level of Recommendation*
Metacognitive strategy training (self-monitoring and self-regulation) is recommended for the treatment of mild-moderate deficits in executive functioning, including impairments of emotional self-regulation, during post-acute rehabilitation after TBI. Metacognitive strategy training may incorporate formal protocols for problem solving and goal management, and their application to everyday situations and functional activities, during postacute rehabilitation after TBI.	Practice Standard
Metacognitive strategy training should be incorporated into occupation-based treatment for practical goals and functional skills for patients with mild-moderate deficits in executive functioning after TBI and stroke.	Practice Guideline
Explicit (verbal-and-video) performance feedback should be considered to as a formal component of Metacognitive strategy training during postacute rehabilitation for individuals with impaired self-awareness after TBI.	Practice Guideline
Group-based interventions may be considered for remediation of mild-moderate deficits in executive functioning (including deficits in awareness, problem solving, goal management and emotional regulation) during post-acute rehabilitation after TBI.	Practice Option
For patients with severe cognitive (executive) deficits after stroke or TBI,	Practice Option

including limitations of emergent awareness and independent use of compensatory strategies, the use of skill-specific training including errorless learning may be considered to promote performance of specifically trained functional tasks, with no expectation of transfer to untrained activities	
Metacognitive strategy training may be considered as a component of occupation-based treatment during acute rehabilitation to reduce functional disability for patients with cognitive impairment after stroke.	Practice Option

Table 7. Recommendations for comprehensive-holistic neuropsychological rehabilitation

Intervention	*Level of Recommendation*
Comprehensive-holistic neuropsychological rehabilitation is recommended during postacute rehabilitation to reduce cognitive and functional disability for persons with TBI or stroke, regardless of severity or time post injury	Practice Standard
Multi-modal, computer-assisted cognitive retraining *with the involvement and direction of a rehabilitation therapist* is recommended as a component of neurorehabilitation for the remediation of attention, memory, and executive function deficits following stroke or TBI. Computer-assisted cognitive retraining programs should stimulate the cognitive domains of interest, adjust task difficulty based on patient's level of performance, and provide feedback and objective performance data	Practice Guideline
Integrated treatment of individualized cognitive and interpersonal therapies is recommended to improve functioning within the context of a comprehensive neuropsychological rehabilitation program, and facilitate the effectiveness of specific interventions. Such interventions should be goal directed and emphasize individualized client centered goal setting to promote enhanced residential independence and occupational functioning	Practice Option
Group-based interventions may be considered as part of comprehensive-holistic neuropsychological rehabilitation to improve functional	Practice Option

awareness, strategy use, functional independence and psychological well being after TBI or stroke	