Brain Injury, February 2007; 21(2): 161–200

informa
healthcare

Cognitive interventions post acquired brain injury

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(Received 30 June 2006; revised 6 December 2006; accepted 8 January 2007)

Abstract

Objective: Cognitive rehabilitation represents a substantial portion of rehabilitative efforts put forth in increasing independence following an acquired brain injury.

Main outcomes and results: This review examined four major areas of cognitive therapy including: attention/concentration, learning and memory, executive functioning, and general cognitive rehabilitation approaches. In total, 64 studies were evaluated throughout the four major areas, which provided the evidence-base for 18 conclusions. The majority of the conclusions were based on moderate and limited evidence, however three strong and one conflicting conclusions were made.

Conclusions: Future research should explore functional outcome measures and long-term effects of treatment interventions through follow-up.

Keywords: *Attention, brain, brain injuries, craniocerebral trauma, cognition, cognition disorders, cognitive therapy, drug therapy, evidence-based medicine, memory, rehabilitation*

Introduction

Acquired brain injury (ABI) can be defined as 'damage to the brain that occurs after birth and which is not related to congenital disorders, developmental disabilities, or processes that progressively damage the brain' [1]. By this definition, ABI encompasses a wide variety of disorders of varying etiologies (e.g., traumatic brain injury (TBI), tumour, cerebrovascular accident, infection, etc). As a result, most research studies comprise a heterogeneous group of participants all of whom could be grouped under the umbrella term of 'acquired brain injury'. Even if one were to examine traumatic brain injury separate from other forms of ABI, substantial variability across participants remains (e.g., TBI due to acceleration/deceleration forces of a motor vehicle accident has differential effects on brain structure and function and hence cognitive functioning than TBI due to a more static injury).

When examining the efficacy of intervention studies, cross-study comparisons become difficult not only as a result of the heterogeneity of the population under investigation but also due to the diversity of cognitive interventions and outcome measures employed. Factors such as time since injury and appropriate outcome measures need to be adequately controlled so as not to confound spontaneous recovery or practice effects respectively, with treatment efficacy [2, 3].

What is known is that cognitive deficits are common following ABI in that 'it interferes with rehabilitation efforts, is enduring/chronic and results in a greater negative impact on quality of life than physical disabilities alone' [4]. As a result, cognitive

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ISSN 0269–9052 print/ISSN 1362–301X online
DOI: 10.1080/02699050701201813

rehabilitation represents a substantial portion of rehabilitative efforts put forth in increasing independence following an acquired brain injury. Although the term 'cognitive rehabilitation' is commonly used, there is no consensus on a definition. For the purposes of this paper, cognitive rehabilitation will be defined as 'efforts to promote maximal adaptive cognitive functioning in patients with neurologically induced cognitive deficits' [4].

The following paper will address both cognitive rehabilitative programs as an intervention as well as specific approaches that focus on particular cognitive domains (e.g., memory, attention, etc), and pharmacological interventions. The purpose of this evidence-based review was to investigate the efficacy of interventions or treatments for moderate to severe acquired brain injury using five levels of evidence listed below.

Methods

A comprehensive search of four electronic databases (CINAHL, EMBASE, MEDLINE and PsycINFO) was conducted covering the years 1980–2006. All published literature that evaluated the effectiveness of any treatment or intervention related to the rehabilitation of moderate-to-severe acquired brain injury was searched. Additional references that were hand-searched using the bibliographies of selected articles were also included.

The methodology and assessment of articles, using the PEDro (5) and Downs and Black (6) scoring systems for randomized controlled trials and the Downs and Black tool for non-randomized trials, was described in an earlier article in this issue. There were five levels of evidence used to summarize the findings. These included:

- *Strong Evidence*: The findings are supported by the results of two or more RCTs of at least fair quality ('fair' quality defined as a PEDro score of four or higher).
- *Moderate Evidence*: The findings are supported by a single RCT of at least fair quality.
- *Limited Evidence*: The findings are supported by at least one non-experimental (prospective and retrospective controlled trials, single group interventions, etc.).
- *Consensus Opinion*: In the absence of evidence, agreement by a group of experts on the appropriate treatment course. Consensus opinion is regarded as the lowest form of evidence. As such, it is arguably not considered evidence at all.
- *Conflicting Evidence*: Disagreements between the findings of at least two RCTs or where RCTs are not available between two non-RCTs. Where there are more than four RCTs and the results of only one was conflicting, the conclusion was based on the majority of the studies, unless the study with conflicting results was of higher quality.

Results

Attention, concentration & information processing speed

Examining the efficacy of rehabilitation of attention deficits following a brain injury is complicated by a number of factors. First, there is no consensus regarding a definition of attention. Is it a general construct or does it reflect more specific subcomponents or systems of functioning (e.g., sustained, divided, focused, selective, vigilance, speed of information processing, etc)? Second, different researchers and clinicians will report using the same or similar tests to measure different aspects of attention. Third, a study may use the same outcome measures repeatedly, thereby confounding practice and treatment effects. Finally, comparing the efficacy of various remediation efforts is also complicated by cross-study variability in treatment duration (e.g., from 30 minutes once daily for five days to five hours every day for six weeks).

Overall, 11 studies were reviewed that examined the effects of intervention on attention and information processing speed following moderate-to-severe ABI. Four of those studies examined pharmacological intervention while the remaining seven reported on behavioural indices of intervention (e.g., drill and practice).

Pharmacological intervention. Three RCTs investigated the effects of Methylphenidate (MP), a psychostimulant, on attention with a total of 57 patients with traumatic brain injury. Whyte et al. [7] indicated that the Methylphenidate treatment led to significant improvements for speed of processing, attentiveness during individual work tasks and caregiver ratings of attention. Similar findings were reported by Plenger et al. [8] and Kim et al. [9].

The effects of Donezepil on attention for patients following TBI were explored [10]. For the 18 post-acute TBI patients studied, Donezepil resulted in a significant increase in scores on tasks of sustained attention and short-term memory and these results were sustained following the washout period (Table I).

Conclusions regarding pharmacological intervention. Results from three RCTs provided *strong* evidence that Methylphenidate helps to improve the speed of cognitive processing and attention during the active phase of treatment.

Table I. Effects of pharmacological interventions on cognitive function.

Author/Year/Country/ Design/PEDro/D&B	Eligibility criteria	Study methods	Outcome measures	Results
Whyte et al. 2004 [7] USA RCT D&B = 19 PEDro = 8	Inclusion: Age range between 6 and 60 years; history of non-penetrating TBI of at least moderate severity at least 3 months before enrolment; ability to perform tasks for 10–15 minutes independently and available to attend the project five days/week for six weeks. Exclusion: Currently hospitalized; pregnancy; History of premorbid neurological disease; psychosis; major affective disorder; mental retardation; ADHD; substance abuse; currently taking psychotropic medications other than anticonvulsants; impairments in vision, hearing, or motor function.	Double blind crossover randomized design. 34 patients were randomly assigned to two groups. Patients in both groups received either placebo or MP 0.3 mg/kg/dose twice daily for six days a week. The intake of placebo or MP was counter-balanced between groups. Sunday was used as a washout period before the crossover to the opposite condition. The program lasted a period of six weeks.	Sustained arousal and attention task 50/50; Sustained arousal and attention task 20/80 (target rate was 20%); Distraction task; Choice Reaction Time Task; Dual task; Sustained Attention to Response Task; Test of Everyday Attention; Inattentive behavior task; Attention ratings.	Of 13 attentional factors, five showed suggestive treatment effect in the pilot sample. Three of these, including speed of information processing, attentiveness during individual work task and caregivers ratings of attention, showed significant treatment effects (p value?). No treatment related effects were observed in divided attention, sustained attention, or susceptibility to distraction.
Plenger et al. 1996 [8] USA RCT PEDro = 5 D&B = 17	Inclusion: Galveston Orientation and Amnesia Test score ≥ 65, Age between 16–65, sustained a moderate to moderately severe TBI (admission GCS of 6 – 12 without bolt placement) or complicated mild TBI (GCS of 13–15 with evidence of cerebral contusion on CT. Exclusion: Previous head injury, history of psychiatric illness, history of drug or alcohol abuse requiring treatment, history of seizures activity or cardiac problems.	23 patients were randomly assigned to one of two treatment conditions: (1) Methylphenidate twice a day, at dose of 0.30 mg/kg, for 30 days; or (2) Placebo for 30 days.	*Functional Outcome:* Disability Rating Scale (DRS) *Orientation:* Galveston Orientation and Amnesia Test (GOAT) *Attention:* Continuous performance test CPT (Vigil), 2 & 7 Test Paced Auditory Serial Addition Test (PASAT) *Digit Span & Attention/concentration:* Wechsler Memory Scale-Revised (WMS-R) *Learning and Memory:* Selective Reminding Delayed Verbal and Visual Memory from the WMS-R *Procedural Memory:* Porteus Maze, Pursuit Roter. Symptom interview and side effects checklist were also administered. Wilcoxon Rank Sum tests were used to analyse the results.	Significant differences in the DRS at 30 days ($p < 0.007$) indicated better outcome for the methylphenidate group. There was no significant change in DRS from the 30 day to the 90-day evaluation for the methylphenidate group (no p value), while this analysis approached significance for the placebo group ($p = 0.10$). Similarly, no significant differences on DRS, Continuous Performance Test or declarative memory were noted between groups. Significant improvement in Continuous Performance Test at 30 days ($p < 0.038$), but not at the 90-day follow up period in the methylphenidate group compared with placebo. Significant improvement in attention at 30 days follow-up in favour of the methylphenidate group ($p < 0.03$).

(continued)

Table I. Continued.

Author/Year/Country/Design/ PEDro/D&B	Eligibility criteria	Study methods	Outcome measures	Results
Kim et al. 2006 [9] Korea RCT PEDro = 6 D&B = 17	Inclusion: Chronic phase of TBI; mild cognitive impairment; no previous brain disorders. Exclusion: Patients with severe motor weakness and psychiatric problems.	18 TBI adults were randomly assigned to one of two treatments: (1) a single-dose 20 mg of methylphenidate; or (2) placebo.	Two tasks measured cognitive function: working memory and visuospatial attention. Response accuracy and reaction time were recorded.	Before treatment, there were no significant differences between groups on measures of response accuracy and reaction time for working memory or visuospatial attention. Following treatment, there was a significant difference in the improvement ratio from T2 to T1 between the groups on reaction time of working memory. There was marginal improvement on the response accuracies measures between groups ($p = 0.07$). On measures of visuospatial attention following treatment, there were no significant differences between groups for reaction time or response accuracy.
Zhang et al. 2004 [10] USA RCT (Cross-over) D&B = 23 PEDro = 7	Inclusion: History of TBI; Attention impairments (as demonstrated by the WMS-III or PASAT); Enrolment from 2-24 months post brain injury; Informed consent. Exclusion: Medical complications; Cognitive and behabioural functioning at level V (confused) or below on Rancho Los Amigos (RLA) Levels of cognitive functioning; Neurologic or psychiatric complications; Concurrent psychotropic medication use; Communication impairments that could interfere with neuropsychological testing.	20 patients were randomly assigned to either one of two groups: (1) Patients received donepezil orally for first 10 weeks, followed by a 4-week washout period, and then placebo for 10 weeks; or (2) Patients received treatment in the reverse order of Group A, receiving placebo first, followed by washout, followed by 10 weeks of oral donepezil. Donepezil was administered at a dosage of 5 mg/day for the first 2 weeks and 10 mg/day for the remaining 8 weeks.	Auditory Immediate Index (AII), Visual Immediate Index (VII) of the Wechsler Memory Scale-III and the Paced Auditory Serial Addition Test (PASAT). Measures were tested at baseline, week 10 and week 24 of intervention.	Significant increases in scores with Donepezil for intragroup comparisons. No statistically significant differences were noted between the groups at 24 weeks on the AII or VII. Similar benefits in favour of donepezil were noted with the PASAT. At the end of the donepezil phase, PASAT scores on four testing rates were significant ($p < 0.001$) compared with baseline of Group A and with the placebo phase in Group B. No significant differences between groups were detected at week 24.

Moderate evidence that Donezepil improves attention and short-term memory also exists and results were sustained during washout.

Drill and practice

Drill and practice exercises were traditionally paper-and-pencil tasks that were given repeatedly. With the increase in computer technology and availability, specific computerized attention tasks have been developed with the goal of retraining attention through repetition of various attentional tasks (Table II).

Two RCTs explored the influence of drill and practice techniques on attentional functioning for patients following a brain injury. Novack et al. [11] randomly assigned 44 individuals with TBI to receive one of two treatments: (i) a focused hierarchical stimulation program (attention skills), or (ii) an unstructured intervention program (control group). Both groups received 30 minutes of 'cognitive remediation' five times a week. Results indicated that both groups performed significantly better at discharge compared to admission but no between group differences were observed. Niemann et al. [12] randomly assigned 29 patients with TBI into two groups: attention group (computerized tasks of attention) or a memory group (prospective tasks of memory aides). Both groups showed improvement when their post-test scores were compared to pre-test scores. However, the attention group improved significantly over the memory group on measures of attention.

Two studies [13, 14] examined whether individuals with TBI would show improvement in attention (as measured by the PASAT) after exposure to the Attention Process Training (APT; a computerized series of attention tasks). Both studies did report improvement following the intervention; however, the control group in Park et al. [13] also showed significant improvement on the PASAT indicating practice effects were not well controlled. Sohlberg and Mateer [14] also reported that the level of 'recovery' was related to the severity of the deficit (e.g., mild to moderate attention deficits increased to normal levels whereas those with severe impairments improved to the mildly impaired range). It is worth noting that p values were not provided within these analyses.

One prospective controlled trial [15] studied 10 participants and found that significant phase effects from baseline to training reflected a spontaneous recovery or practice rather than a treatment effect. In another study using four male patients with TBI, Gansler and McCaffrey [16] found no clinically significant improvement in attention measures, neuropsychological variables, psychological characteristics, activities of daily living or subjective ratings following a four week intensive hierarchically ordered attention program based on Posner's four component model.

Conclusions regarding drill and practice. There is *moderate* evidence to suggest that specific structured training programs are not effective for improving attention following moderate to severe brain injury.

Dual-task training

One RCT and one prospective controlled trial investigated the effect of dual-task training on the speed of processing following brain injury with a total of 32 patients. Fasotti et al. [17] randomly assigned 22 patients to receive either: (i) a Time Pressure Management (TPM; self management strategies) treatment group for 1 hour sessions, three times a week, or (ii) a concentration training control group for 2–5 hours/week over the course of 3–4 weeks. Findings revealed improvement in performance occurs across both groups but that TPM produced greater gains than the control group and appears to generalize to other measures of speed and memory.

A computerized dual-task was administered to 19 patients and 19 uninjured control subjects [18]. It was demonstrated that reaction time for patient groups was significantly slower than control groups and that patient groups demonstrated significantly greater dual-task cost (i.e., slower performance in dual-task conditions than single task conditions), but that with training performance improved over sessions at a faster rate than controls so that by the last session no significant differences existed in reaction time for patient and controls. Carry-over effects were also observed on measures of executive functioning following training (Table III).

Conclusions regarding dual-task training. Based on a single RCT, there is *moderate* evidence that dual-task training on speed of processing is an effective intervention for patients with brain injury.

Learning and memory

Thirty studies were identified that examined the interventions used to improve learning and memory following acquired brain injury. According to this literature, there are two main approaches to rehabilitation: (i) restoration or retraining of the function, and (ii) compensation. Compensation refers to any technique used to aid in the recovery of memory impairment following brain injury. These techniques include external and internal aids.

Table II. Influence of drill and practice on attentional functioning.

Author/Year/ Country/Design/ PEDro/D&B	Eligibility criteria	Study methods	Outcome measures	Results
Novack et al. 1996 [11] USA RCT D&B = 15 PEDro = 5	Inclusion: Ability to communicate. Exclusion: Not explicitly stated, however 17 potential participants were excluded because they did not meet the matching variables of age, education, or time since injury.	44 participants were randomized to receive one of two treatments: (1) Focused hierarchical stimulation program whereby treatment was conceptualized on the basis of hierarchy of attentional skills; or (2) Unstructured, non-sequential, nonhierarchical intervention program. Each patient was assigned to 30 minutes of cognitive remediation five times a week.	*Cognition:* Digit Span Forward, Digit Span Backward, Digit Span Total, Mental control of subtests of the Wechsler Memory Scale-Revised (WMS-R), Simple and Choice Reaction Time, FIM (ADLs), FIM. *Neuropsychological Test Measures*: Logical Memory I, Logical Memory II, Sentence Repetition, Judgment of Line Orientation, Trail Making A, Trail Making B, Arithmetic subtest of Wide Range Achievement Test-Revised, Visual imperception.	No significant differences noted in attentional skills, functional skills or general cognitive abilities, or activities of daily living between groups. Overall significant effect of time with all subjects performing significantly better at discharge than on admission ($p < 0.0001$).
Niemann et al. 1990 [12] USA RCT PEDro = 5 D&B = 17	Inclusion: Age range 6–60 years; Moderate to severe injury severity with a minimum coma duration of 1 hour; Chronicity ranging from 12–72 months; No evidence of severe disorientation and confusion (GOAT score ≥ 75, DRS score ≥ 100); No severe aphasia; Sufficient vision to read text on a computer screen; One functional hand; No substance abuse since the injury; No premorbid history of psychiatric disorders resulting in hospitalizations. Exclusion: Not specified.	29 patients were randomized into one of two groups: (1) Attention training (experimental group) included three major components: visual, auditory, (what is the third component) or (2) divided attention (simultaneous audiovisual presentations). Task duration varied from 5–10 minutes and all visual tasks were computerized. The three major components were further subdivided into focused and alternating attention tasks: focused tasks consisted of correct identifications of targets and distractions. Task difficulty was varied systematically by changing several aspects of the task such as the number of targets and distractors, the degree of similarity between targets and distractors and interstimulus interval (auditory task only). Training lasted nine weeks with two 2-hour per week for both groups.	*Baseline measures*: Attention Test d2; Paced Auditory Serial-Addition Task- Revision; Divided Attention Test; Trail Making Test Part B; Rey Auditory Verbal Learning Test- Modified; Block Span Learning Test; *San Diego Neuropsychological Test Battery* (selected tests): Ruff 2 & 7 test; Logical Memory subtest of the Wechsler Memory Scale; Ruff-Light Trail Learning test. Baseline measures administered at 7–9 day intervals three times before intervention, six times during intervention and twice following intervention.	The attention group improved significantly more than the memory group on four measures of attention (all versions of the Trail Making Test Part B) ($p < 0.025$).

Ponsford and Kinsella 1988 [15] Australia Prospective controlled trial D&B = 13	Inclusion: Patients aged 16–45 years with no history of previous neurological or psychiatric disturbance; a period of posttraumatic amnesia exceeding 24 hours; at least < 12 months postinjury; sufficient visual acuity and exhibited impaired performance on psychomentric measures of speed. Exclusion: Not specified.	10 patients with closed-head injury admitted for rehabilitation participated in a remedial programme for attentional deficits. These patients were matched with 16 orthopaedically-injured motor accident rehabilitation patients.	*Psychometric measures of speed of information processing*: Four-choice reaction time task; Symbol Digit Modalities Test; Two-letter cancellation task. WAIS/NHAIS Similarities subtest; Rating Scale of Attentional Behaviours; 30-minute video used to assess performance of patient on overt attentional behaviours such as distractibility and ability to sustain attention to a task.	Rating Scale of Attentional Behaviours showed no significant differences between groups. Results of the video did not show any significant group or phase effects and no significant group x phase interaction. Patients showed a gradual improvement across all phases in all measures revealing spontaneous recovery.
Park et al. 1999 [13] Canada Retrospective controlled trial D&B = 16	Inclusion: Participants with evidence of TBI; Results suggesting attention deficit; Clinical judgment that the patients might benefit from attention process training, no outstanding medical problems and consent. Exclusion: Not specified	23 TBI patients received attention process training (APT), a programme enabling practice in a variety of tasks requiring several different types of attention. These patients were matched to a control group ($n = 23$) from a previous study. The training programme was designed to last a total of 40 hours.	Beck Depression Inventory (BDI); Paced Auditory Serial Addition Task (PASAT).	BDI results indicated that TBI patients were moderately depressed before and after training. Both groups improved on PASAT from test one to two (treatment at $p < 0.01$ and control at $p < 0.001$). Performance on consonant trigrams test was higher after training for treatment group, but no significant change for control group from test one to two.
Gansler and McCaffrey 1991 [16] USA Collection of case studies No score	Inclusion and exclusion criteria not specified.	Four patients participated in this A-B-A study design, whereby the initial A-phase consisted of a four-week pre-treatment baseline. Phase B was the attentional remediation program conducted over the next consecutive eight weeks. The second A-phase took place following the end of the remediation period for four weeks.	*Attentional measures*: These assessments were derived from Posner's (1975) hierarchical four-component model of attention, which consists of four levels of attentional processes including: tonic awareness, phasic awareness, selective attention and vigilance/sustained attention. *Activities of Daily Living*: Self-report measures were used along with ratings by a significant other. Measures examined the subjects' ability to concentrate on their ADLs, satisfaction in performing the ADLs, and the quality of their performance on ADLs.	Attentional measures: No systematic change from pre-to-posttreatment in simple reaction time, choice reaction time or reaction time with a warning for three of four patients. Overall, only one patient of four demonstrated an increases attentional capacity.

(*continued*)

Table II. Continued.

Author/Year/Country/Design/PEDro/D&B	Eligibility criteria	Study methods	Outcome measures	Results
			Psychological variables: Beck Depression Inventory (BDI), The State-trait Anxiety Inventory and the State-trait Anger Inventory. *Neuropsychological battery*: Wechsler Memory Scale (Form I) – Russell's Revision, Paired-Associate subtest of the Wechsler Memory Scale, Trail-Making Test, Minute Estimation Test, Thurstone Word Fluency Test, Grooved Pegboard Test and the Picture Arrangement, Block Design, Arithmetic, Digit Span and Similarities subtest of the WAIS-R.	
Sohlberg & Mateer 1987 [14] USA Collection of case studies No score	No specified inclusion and exclusion. Participants were randomly selected from a consecutive series of admissions to the Center for Cognitive Rehabilitation.	Four brain-injured individuals participated in the attention treatment program (APT). Five levels of attention were addressed in the therapy model: focused attention, sustained attention, selective attention, alternating attention, and divided attention. Each participant received four to eight weeks of training. Concurrent intervention in the areas of daily living, prevocational and psychosocial skills were employed.	Paced Auditory Serial Addition Task (PASAT); Spatial Relations Subtest (SR) from the Woodcock Johnson Psychoeducational Battery.	All four participants demonstrated gains in attention following the initiation of attention training.

Table III. Influence of dual-task training on speed of processing.

Author/Year/Country/ Design/PEDro/D&B	Eligibility criteria	Study methods	Outcome measures	Results
Fasotti et al. 2000 [17] Netherlands RCT D&B = 19 PEDro = 5	Inclusion: Evidence of slowed speed of information processing; Wechsler Adult Intelligence Scale IQ equal or superior to 75; Age between 18 and 50 years; No severe intellectual, aphasic, agnostic, or personality disorders; Patients had to state explicitly their interest in being a part of the study. Exclusion: Not specified.	22 closed head injury patients were randomly assigned to one of two conditions: (1) 12 patients received Time Pressure Management (TPM) training and (2) 10 control subjects received concentration training consisting of several verbal suggestions selected from existing memory training program.	*Effects of TPM training evaluated using:* "Story" and "computer" tasks. A behavioural observation list was used to assess the use of strategies. *Neuropsychological battery:* 15-word test; Rivermead Behavioural Memory Test; an Auditory Concentration Test; PASAT; Visual Choice Reaction Time Task. *Psychosocial well-being:* Scale for Subjective Well-being for the Elderly (SSWO); Trauma Complaints List; Dutch Self-esteem questionnaire. General activity questionnaire assessed # of leisure activities and social contacts.	For both tasks, main time effects showed that levels of managing performance increased significantly after training. Strategy training group took significantly more managing steps than the control group after training (as demonstrated by group time effects), but the effect only remained stable after 6 months in the HG task. No significant changes were found between pre- and post-training measures in psychosocial wellbeing.
Stablum et al. 2000 [18] Italy Prospective controlled trial D&B = 22	Inclusion criteria: evidence of an acceleration-deceleration closed head injury (CHI), a normal CT, no previous history of mental retardation, psychiatric illness, previous head injury, alcoholism, or drug use, no residual motor deficit, not seeking financial aid, not pursuing litigation, and good recovery. Controls with a history of alcoholism, mental retardation, neurological disease or psychiatric disorder were excluded.	19 patients (10 closed-head-injured (CHI) patients and nine anterior communicating artery (AcoA) aneurysm patients) were evaluated using a dual-task paradigm in two studies. 19 uninjured participants were used as controls. The CHI study consisted of an initial assessment followed by a five-session intervention with Dual Task. Retesting was administered following the treatment, and a 3-month follow-up was conducted. The AcoA Aneurysm study involved an initial assessment, a five-session intervention with Dual Task, and retesting following treatment. 3- and 12-month follow-ups were conducted.	*CHI study* *Neuropsychological battery:* Raven Mental Control; Corsi Block Tapping; Digit Span (Forward and Backward); Digit-Symbol, Arithmetic Reasoning; Attentive Matrices; Tower of London; Phonemic Verbal Fluency; Elithorn's Perceptual Maze test; Wisconsin Card Sorting Test (WCST); PASAT; and the Dual-task assessment. *AcoA Aneurysm study* Raven; WCST; Trail Making Test; PASAT; WAIS; Verbal Reasoning; Story Recall; Elithorn Maze Test; Corsi Block Tapping; Spatial Supraspan; Attentive Matrices; Digit Span (Forward and Backward); Verbal Span; Phonemic Verbal Fluency; Phrase Construction; Continuous Performance Task; Dual-task assessment.	*CHI study* Significant group main effect ($p < 0.001$) in favour of the treatment group. *AcoA Aneurysm study* Significant group main effect ($p < 0.007$) in favour of the treatment group.

External aids

External aids help to improve memory impairment following acquired brain injury by use of the external means of recording (i.e., encoding) and accessing information (storage and retrieval).

Ten studies investigated the effects of external aids for enhanced memory following acquired brain injury (Table IV). Two RCTs used different external memory aids to compare outcome of participants with brain injury. Watanabe et al. [19] investigated the use of a calendar for 30 severe TBI patients and found that there were no significant effects as noted on the Temporal Orientation Test (TOT) outcome measure. Ownsworth and McFarland [20], on the other hand, randomly assigned 20 ABI patients to receive either: (i) the use of a diary as external aid only (DO), or (ii) the use of a diary coupled with the self instructional training (DSIT) for 4 weeks of treatment. Results showed that during treatment, patients in DSIT consistently made more diary entries, reported fewer memory problems and made more positive ratings associated with treatment efficacy relative to DO group.

Using a memory notebook as the external memory aide, Schmitter-Edgecombe et al. [21] assigned eight patients with severe ABI with memory impairment into a notebook-training group or an interpersonal support group (control). Results indicated that on neuropsychological measures of memory functioning no group differences were found. However on an everyday memory failures questionnaire, performance improved following treatment, although it was not maintained at 6-month follow-up. Zencius et al. [22] found that memory notebook training was found to increase the number of homework components correctly completed compared to baseline performance.

A number of studies (single group interventions) have examined the use of technological aides to enhance memory. Wade and Troy [23] found that memory was improved in patients using a mobile phone pre-programmed to remind participants of individualized events (e.g., upcoming appointments, reminders to take medication etc). Wright et al. [24, 25] examined the effect of two pocket computer systems using 3 memory aides (appointment diary, notebook and a to-do-list) and reported no significant difference between the two systems and/or use of memory aides. Interestingly they indicate that those who were familiar with using such systems/aides made significantly more entries. Use of a portable paging system [26] and hand-held recorders [27] resulted in reducing everyday memory problems and in increasing retention of therapy goals, respectively. Burke et al. [28] reported that use of a 'patient locator and minder' (PLAM) electronic system on an inpatient unit resulted in significantly fewer prompts being made, and more appointments being attended on time, than when nursing staff verbally prompted patients.

Conclusions regarding external aids. There is *strong* evidence surrounding the effectiveness of external aids as a compensatory strategy for memory impaired individuals for functional day-to-day memory problems. However results do not necessarily indicate improved underlying memory abilities and the long-term effect has not been adequately demonstrated.

Internal aids

Internal aids generally refer to mnemonic strategies that are taught in order to enhance encoding and later recall of information. Researchers have demonstrated that increasing the saliency of features encoded (either by verbal and/or visual elaboration) results in improved performance during recall (i.e., better retention) (e.g. [29–31]). Fourteen studies, including three RCTs, evaluated the effectiveness of internal aids to help improve memory impairment post-brain injury (Table V).

Twum and Parente (32) randomly assigned 60 patients with TBI to one of three treatment groups and a control group: (i) no imagery/verbal labeling, (ii) imagery/verbal labeling, (iii) imagery/no verbal labeling, or (iv) no imagery/no verbal labeling (control group). Results indicated that mental imagery and verbal labeling were both effective in improving performance during learning and recall of information. Use of mnemonic strategies (verbal and/or visual) has also been supported in studies using single group intervention designs (e.g., [33, 34]) and a RCT study [35]. Of interest is that Ryan and Ruff [35] reported differential effects of mnemonic strategies dependent on level of impairment. That is, performance was enhanced for mildly impaired participants only; severely impaired patients did not benefit from visual imagery.

Memory strategy training was compared to drill and practice training, and a control group that did not receive treatment, for 39 individuals with severe brain injury randomly assigned to one of the three groups [36]. Although results demonstrated that no differences existed between treatment groups on reaction time, it was found that patients in the memory strategy group performed better than the other groups (although no p value was included for this result). A follow-up of this study, Milders et al. [37], indicated that the differences between groups were not maintained at four years follow-up.

Table IV. The use of technological aids to enhance memory.

Author/Year/Country/ Design/PEDro/D&B	Eligibility criteria	Study methods	Outcome measures	Results
Watanabe et al. 1998 [19] USA RCT D&B = 20 PEDro = 3	Included were patients consecutively admitted to brain injury impatient rehabilitation units. Patients with aphasia or visual deficits severe enough to make them unable to see in-room calendars were excluded.	30 brain-injured patients were randomly assigned to one of two treatment conditions. One group received in-room calendars ($n = 14$), while the second group did not receive in-room calendars ($n = 16$).	Temporal Orientation Test (TOT). Assessed daily or until two consecutive normal scores were obtained.	No significant changes in TOT scores suggesting that the presence of in-room calendars following brain injury does not help to improve re-orientation.
Ownsworth & McFarland 1999 [20] Australia RCT D&B = 18 PEDro = 3	No inclusion or exclusion criteria specified.	20 brain-injured individuals were randomly assigned to receive one of two treatment conditions: (1) 10 subjects were given a diary alone (DO) as a compensatory method of treatment; and (2) 10 subjects were given a diary, in addition to Self-Instructional Training (DSIT).	Self Report Questionnaire; Rivermead Behavioural Memory Test; WMS-R subtests (Figural Memory, Visual Paired Associated I, Verbale Paired Associates I, Digit Span and Visual Memory Span); Weekly Mood Questionnaire.	During treatment phase, DSIT group regularly made more entries, reported fewer memory problems and rated the treatment more positively than the DO group. DSIT group maintained their use of the diary strategy to a greater extent than DO subjects.
Schmitter-Edgecombe et al. 1995 [21] USA Prospective controlled trial D&B = 22	Included patients aged between 17 and 55, >grade 10 education, length of coma >2 days, age at injury >15, time since injury >24 months, IQ >75, dementia rating scale (DRS) score >133, Wechsler Memory Scale – Revised (WMS-R) standard score <89, negative premorbid history of learning disability, no psychiatric diagnosis and not actively using an external memory aid. Exclusion not specified.	Eight individuals having sustained a severe closed head injury (CHI) were allocated to receive one of two treatments: (1) notebook training ($n = 4$); or (2) supportive therapy ($n = 4$). Once both groups were formed, the treatment group was chosen randomly.	*Laboratory-based recall tests*: Logical Memory I and II scales: Visual Reproduction I and II scales *Laboratory-based everyday memory tests*: Rivermead Behavioural Memory Test; Retrospective questionnaires of everyday memory failure; Everyday Memory Failures (EMF) Questionaire Symptom Checklist 90-Revised	No significant differences between treatment and control group for lab-based recall, lab-based everyday memory, retrospective report of EMF, or symptom distress indicators. Significant difference between treatment and control group for observed EMF score post-treatment ($p < 0.05$), but not significant at 6 month follow up. Treatment group improved significantly from baseline on retrospective report of EMF score at 6 month follow up ($p < 0.05$) but not at post treatment. Treatment group had significantly fewer observed EMFs from baseline at post-treatment and at 6-month follow up.

(*continued*)

Table IV. Continued.

Author/Year/Country/ Design/PEDro/D&B	Eligibility criteria	Study methods	Outcome measures	Results
Wright et al. 2001 [24] UK Single group intervention D&B = 10	No inclusion or exclusion criteria specified.	Two computer organizers of different format and design were compared and counter balanced over the designs with a 1-month gap in between machines in 12 TBI patients.	*Psychometric profiles*: Nation Adult Reading Test (NART); Speed and Capacity of Language Processing Test (SCOLP); Rivermead Behavioural memory Test (RBMT); Behavioural Assessment of Dysexecutive Syndrome (BADS).	Appointment diary was rated as more useful and used more often than the other memory aids. Diary features most often used were auditory alarms (54% total entries) and repeated entries (46% total entries). Diary use did not correlate with the psychometric tests.
Wilson et al. 1997 [26] UK Single group intervention D&B = 14	Inclusion: Not specified. Exclusion: Not specified. Implied that all patients have organic memory problems (neurologically impaired).	15 patients were exposed to NeuroPage, a new memory aid. The experimental design was ABA. The first A phase was baseline, B phase was for treatment and the final A phase was for post-treatment baseline.	Odds ratio test; Mean percent success.	Mean % success for the whole group in the baseline phase was 37.08 and the mean success for treatment was 85.56. Ratio test showed that all subjects improved and benefited significantly from NeuroPage. Mean % success post-treatment indicated more success after the use of NeuroPage.

Hart et al. 2002 [27] USA Single group intervention D&B = 13	Included patients involved in comprehensive treatment, documented and confirmed memory impairment, absence of severe language deficits Exclusion not reported.	10 patients having sustained a moderate to severe TBI were enrolled in either the previously noted community re-entry program ($n = 4$) or the clubhouse day program ($n = 6$).	Recall of recorded and unrecorded therapy goals. Qualitative interviews were employed toward the end of the program.	Recorded goals were recalled better than unrecorded goals ($p < 0.001$) Cued recall was superior to free recall for both recorded and unrecorded goals ($p < 0.03$).
Burke et al. 2001 [28] USA Single group intervention D&B = 18	Inclusion: Patients aged 18–75 with diagnosed brain injury; Functional hearing; Sufficient functional vision and adequate mobility (walking or with a wheelchair). Exclusion: Patients with agitated behaviour.	The use of a patient locator and minder (PLAM) system was used on five ABI patients to assist in their adherence to therapy schedules.	Prompts and arrival time Baseline period of staff intervention were compared with those obtained while patients used the Patient Locator and Minder (PLAM) device.	All patients showed improvement in response time when using PLAM when compared to baseline ($p < 0.001$). Average number of human prompts for each activity significantly declined while using PLAM ($p < 0.0005$). Number of sessions requiring no prompting increased.
Zencius et al. 1991 [22] USA Collection of case studies No score	No inclusion or exclusion criteria specified.	Four TBI patients received memory notebook training for two homework assignments per week.	Number of correctly prepared homework assignment components.	Intervention of memory notebook training increased the number of correctly completed components from baseline for all participants.
Wade & Troy 2001 [23] UK Collection of case studies Not scored	Included patients who demonstrated memory impairments in daily living following brain injury and needed to carry out activities independently.	Five patients received a mobile phone as a memory prompt. Each participant was asked to identify four or five target areas where a reminder would be beneficial.	Individual diaries were used by the participant (or caregiver) to document how often identified targets were remembered independently.	All participants demonstrated that using the mobile phone as a memory aid was effective in increasing self-initiated behaviours.

Table V. The use of internal aids to enhance memory.

Author/Year/Country/Design/PEDro/D&B	Eligibility criteria	Study methods	Outcome measures	Results
Twum and Parente 1994 [32] USA RCT D&B = 15 PEDro = 3	Not explicitly stated but the following were implied: patients aged 18–24 who suffered traumatic brain injury (TBI) and who were in a coma for at least 3 weeks following injury.	60 brain-injured patients received both verbal and visual paired associates training tasks and were randomly assigned to one of four conditions: (1) No imagery or verbal labeling; (2) No imagery, coupled with verbal labeling; (3) Imagery and no verbal labeling; or (4) A combination of imagery and verbal labeling.	Verbal Paired Associates (VerPA) task and Visual Paired Associates (VisPA) task from the Wechsler Memory Scale- Revised (WMS-R).	Overall significant main effect of mental imagery instructions ($p < 0.0001$). There was a significant main effect of verbal labelling instructions on the VisPA ($p < 0.0001$).
Ryan & Ruff 1988 [35] USA RCT D&B = 18 PEDro = 3	Elapsed time since injury between 1–7 years, medical and CT documentation of serious head trauma, expressive and receptive language ability that allows for interpersonal communication, at least one functional hand, adequate visual acuity allowing for discrimination of letter and other stimuli, age between 16–65 years, motivation and availability for a 14 week period, no premorbid history of schizophrenic illness or other neuropsychiatric disturbance.	20 patients were divided into treatment and control groups according to score on Dementia Rating Scale (>133 mild, <134 moderate) received either attention and spatial integration exercise (experimental) or psychosocial treatment (control) over a six week treatment period (4 days/week, 5.5 hours/day).	Benton Visual Retention Test (BVRT); Rey Osterieth Complex Figure Test (CFT); Taylor Complex Figure; Selective Reminding Test (SRT); Ruff Light Trail Learning Test (TLT); Wechsler Memory Scale logical memory subtest (WMS).	Both groups improved significantly over time ($p < 0.05$). The experimental group did not show significantly greater improvement when compared to control group (no p value reported). No significant differences between groups on any of the outcome measures. Subjects with mild neuropsychological impairments benefited more from memory remediation when compared to more severely impaired patients ($p < 0.001$).
Berg et al. 1991 [36] Netherlands RCT D&B = 13 PEDro = 4	Inclusion: Not specified. Exclusion: Not specified.	$N = 39$. Two treatment groups and one control group. 15 patients received memory strategy training while 8 patients received drill and practice training and eight patients acted as control.	*Memory tests*: 15 Words Test, Face-Name Learning Test, Shopping List. *Control tasks*: Four-choice reaction time task (28 items) and four-choice reaction time task with distraction (28 items). *Subjective Reports*: Memory Complaints Questionnaire, The Evaluation Questionnaire.	Patients from the memory strategy, training group performed. significantly better at follow-up than the other groups.

Milders et al. 1995 [37] Netherlands Follow-up of RCT D&B = 13 PEDro = 4	Inclusion: Not reported. Exclusion: Not reported.	This is a follow-up to Berg et al. (1991). 31 patients were divided into one of three conditions: (1) Memory strategy training group, (2) Drill and practice training and (3) No training (control) group.	*Memory tests*: 15 Words Test, Face-Name Learning Test, Shopping List. *Control tasks*: Four-choice reaction time task (28 items) and four-choice reaction time task with distraction (28 items). *Subjective Reports*: Memory Complaints Questionnaire, The Evaluation Questionnaire.	Standardized memory sum scores were significantly lower in three patient groups than in the normal control group ($p < 0.05$). Dropout effect on follow-up results was significant ($p < 0.05$). Results for the patients in the memory strategy, training group were significantly lower than demonstrated in Berg et al. (1991). Patients in the Drill and Practice group improved significantly. There was no longer a significant difference demonstrated between groups.
Tailby & Haslam 2003 [55] Australia Prospective controlled trial D&B = 10	Inclusion: Not specified. Exclusion: Patients were excluded if they suffered from depression (as determined by the Beck Depression Inventory-II).	24 participants were divided into three groups based on their performance on the Verbal Memory Index (VMI) sore on the Wechsler Memory Scale- III. The treatment phase was the study phase, which included a new version of errorless learning. Three types of errorless learning (errorful learning, errorless leaning that is examiner-generated and stem completion, and errorless learning that is self-generated) encouraged active participation in learning by the use of elaboration and self-generation. The test phase of the study included explicit learning conditions and implicit testing (stem completion).	Six explicit scores were calculated for each participant (number of items recalled correctly out of 12) in each explicit learning condition at both immediate and delayed testing times.	Two-way ANOVA compared performance under EL (self-reported) and EL (examiner-generated) conditions in the three memory-impaired groups and found an effect of learning, indicating that cued recall performance following self-generated EL was significantly better than that under standard EL conditions. A significant main effect for group was found ($p < 0.001$). It was demonstrated that errorless learning using semantic cues to enable error-free generation of responses by participants produced the best memory recall and the advantage over standard EL method was maintained over time and across groups. A significant main effect of learning condition was found. A significant effect of severity of memory deficit was noted suggesting that performance in standard EL conditions differed between groups. The moderate group performed better than the severe group. No significant difference in performance between the mild and moderate groups.

(*continued*)

Table V. Continued.

Author/Year/Country/ Design/PEDro/D&B	Eligibility criteria	Study methods	Outcome measures	Results
Goldstein et al. 1996 [56] USA Prospective controlled trial D&B = 13	Patients with serious head injuries, memory impairment, absence of dementia and persistent amnesia were included. Excluded were patients with severe aphasia or physical disabilities that prevented computer use.	10 patients from a previous study (Goldstein et al. 1988) and 20 new, comparable patients received computer-assisted training with the Ridiculously Imaged Story (RIS) method. Methodology and some results come from the original study. Ten of the 20 new patients received the computer-assisted version of the face-name training and the other ten patients received the original method. This discrepancy was a result of the substantially longer time it took to develop the computer-related materials for the face-name training than for the RIS method.	Number of words recalled; Free recall. Comparisons between performance;% of correct names recalled after cuing; Number of trials required to learn names.	Both original and computer-assisted methods were significant in word list tasks; Computer-assisted trials were significant for delayed face/name recall. Number of trials to learn list was significant for both original and computer-assisted groups. This study supports the previous finding (from Goldstein et al. 1988) that head-injured patients can learn and utilize these mnemonic techniques and computer-assisted devices may have a beneficial effect.
Milders et al. 1998 [31] Netherlands Prospective controlled trial D&B = 17	No inclusion or exclusion criteria specified.	13 closed-head-injured (CHI) patients underwent memory training consisting of eight sessions (approximately one hour) over a period of four months. The main strategy was to improve learning of new names and was directed at increasing the meaningfulness of people's names. 13 healthy controls were matched to the sample, and did not participate in the treatment.	Name Learning Test; Name-Occupation-Town Learning Test. Famous Faces Naming Test; Digit Span Forwards; Auditory Verbal Learning Task.	Patients' performance at baseline was clearly impaired on all memory tests except for the Digit Span test where the treatment and control group did not differ. ANOVA for patients versus control and baseline versus post-training were significant for group ($p < 0.001$), evaluation moment ($p < 0.001$) and interaction ($p < 0.001$). After training, patients' performance on tests assessing name learning and retrieval improved substantially compared to before training and maintained at 6-month follow up.

Goldstein et al. 1990 [30] USA Prospective controlled trial D&B = 9	Inclusion: Chronic head injury (CHI) patients free of aphasia. Exclusion: Patients with antecedent history of head injury or neuropsychiatric disorder.	16 long-term survivors of closed-head-injury (CHI) (at least one year post-injury) were compared to 14 matched controls. Sixty target words and questions were adapted from Craik and Tulving (1975: Experiment 9). Each participant was administered a Level of Processing paradigm to determine how well they could detect the differences in processing (physical, acoustic or semantic) of to-be-remembered target words. Following the presentation of target words, subjects were assessed.	*Neuropsychological Tests*: Selected subsets of the WAIS-R; Selective Memory Test and Continuous Recognition Memory.	Controls recognized significantly more words than patients and recognition increased from physical to acoustic to semantic processing. Groups did not differ in their ability to correctly answer questions posed during encoding. CHI patients had greater difficulty with tasks requiring holding digits in memory and backward span. Memory performance was lower for CHI patients on all measures of long-term memory.
Constantinidou et al. 1995 [29] USA Prospective controlled trial D&B = 13	Inclusion for patients with closed head injury (CHI): Moderate to severe head injury (determined by three or more of: GCS <12, abnormal initial CT, length of impaired consciousness >20 min, length if acute hospital stay >3 days, positive neurological examination, medical complications secondary to injury, head injury classification according to hospital records. Exclusion for CHI patients: Penetrating head injuries, history or possible co-occurrence of stroke or premorbid neurological or psychiatric history.	$N = 40$. The experimental task consisted of recalling or identifying words and pictures of words under three conditions: auditory, visual and auditory plus visual. Subjects were randomly assigned to one of these three conditions. A practice trial was given and then a target list (List A) was presented five times under each of the three conditions. In trial 6, an interference list (List B) was presented using the same modality. Following presentation of List B, individuals were immediately asked to recall items from List A.	Recall of words on List A under three conditions: auditory (subject listened to word), visual (drawings of objects) and auditory plus visual (drawings of objects and simultaneous naming of objects by examiner).	Significant overall main effect for group, repeated trials, group by trials and modalities. Subjects with closed head injury (CHI) performed poorly in comparison to controls. Both groups performed better with practice trials. A significant main effect for group indicated that the ability of subjects with CHI to retrieve information was significantly affected by the presentation of the interference list compared with the control group. Recognition resulted in improved memory performance as compared with free recall after interference; the simultaneous auditory-visual presentation of information resulting in the highest recognition performance.

(*continued*)

Table V. Continued.

Author/Year/Country/ Design/PEDro/D&B	Eligibility criteria	Study methods	Outcome measures	Results
Glisky & Delaney 1996 [57] USA Prospective controlled trial D&B = 12	Inclusion: Not reported. Exclusion: Not reported.	*Experiment 1*: Eight posttraumatic amnesia (PTA) patients and eight controls were matched for age and education. Subjects participated in three sessions. A different list of 24 words of low to medium frequency were studied and rated for pleasantness of each word. Following a five-minute delay, subjects participated in one of the memory tests: (1) Subjects were given either an implicit stem completion task or an explicit stem-cued recall task; or (2) Participants received the second of the two tests. The order of tests was counterbalanced across subjects. Following the study of the 24-item list, subjects were given two explicit tests of memory, first a test of free recall and then an auditory test of yes/no recognition. *Experiment 2*: In each 12-trial session, eight subjects were presented with the sentence frames minus the target word and were asked to produce the missing word for second session.	*Experiment 1*: Cued recall, free recall and recognition. *Experiment 2*: Number of correct responses for each patient on daily memory tests; Daily GOAT scores; Source memory error.	*Experiment 1*: PTA patients completed more stems with list words after studying those items than in the absence of prior exposure than controls. The priming effect in patients was not significant from that in the controls. Patients were clearly impaired relative to control patients for the explicit stem controlled recall tasks. For free recall and recognition tasks, none of the patients were able to recall any of the list items. PTA patients recognized fewer targets than the controls. *Experiment 2*: All of the patients were able to learn some of the fictitious facts during PTA and demonstrated good transfer to the non-PTA state. Three of the four PTA patients demonstrated at least one source memory error, whereas none of the control subjects made any such errors. No relation could be detected between any of the subject variables and the probability of making a source error.

Ewert et al. 1989 [58] USA Prospective controlled trial D&B = 9	Inclusion: *CHI patients*: Severe closed head injury patients; GCS ≤ 8, aged between 15–50 years at time of injury; No history of neuropsychiatric disorder (including hospitalization for head injury); Patients in PTA persisted over at least the three days of testing. *All participants*: Normal visual acuity, full visual fields, relatively preserved language comprehension. Exclusion: Substance abuse or documented mental subnormality; visual neglect.	32 patients underwent three consecutive days of testing sessions. Four outcome measures were administered during each session. No direct treatment was administered.	Mirror Reading Test; Porteus Maze Test, Pursuit Rotor Test, Recognition Memory Test, Declarative Memory Questionnaire	The CHI patients read two-thirds of the words accurately during PTA, but control subjects performed better. There was a significant improvement in the CHI group in their scores across the first three sessions for the time and blind alley measures. CHI patients increased their percentage of time on target during PTA, confirmed by a significant linear trend across sessions. Recognition of words presented in the reading tests were grossly impaired in the head-injured patients compared with controls.
Thoene and Glisky 1995 [33] USA and Germany Single group intervention D&B = 14	No inclusion or exclusion criteria specified.	12 TBI patients received an intervention focusing on learning name to face associations using three training procedures (mnemonic, vanishing cues, a video presentation).	Number of correct face/name association and retention; Number of trials to criterion.	All patients were able to learn and retain some of the 12 new names and faces after a 3–4 day delay. Criteria were reached by all patients in the mnemonic condition only. Significant main effect for condition, ($p < 0.001$). Number of cues needed to produce the names during training decreased fairly rapidly after a few sessions.
Malec et al. 1991 [34] USA Single group intervention D&B = 13	Inclusion: Clinical or psychometric evidence of persistent memory impairment lasting beyond PTA. Exclusion: Individuals with a Dementia Rating Scale score < 110.	18 brain-injured patients participated in a memory retraining intervention based on the Ridiculous Imaged Story technique using computer-controlled cueing to recall forgotten words. Subjects trained over 15 sessions.	The number of words freely recalled at the end of each session used to evaluate progress. Degree of learning, defined as mean number of nouns correctly recalled during the first four training sessions. Degree of generalization, defined as the mean number of nouns correctly recalled during the first four generalization sessions.	Months post-injury and pre-training performance levels on a list-learning and a selective-reminding task were the only measures significantly ($p < 0.05$) correlated with the learning criterion measure.
Zencius et al. 1990 [59] USA Collection of case studies D&B = 4	No inclusion or exclusion criteria specified.	Six TBI patients were required to extract and recall 6 pieces of job related information from the newspaper want-ads using four different memory therapies (verbal & written rehearsal, acronym formation and memory notebook training).	Correct recall of the six pieces of job related information.	Verbal and written rehearsal memory strategies varied only slightly from baseline values. Memory notebook logging was the most effective in increasing recall of job related information.

Conclusions regarding internal aids. There is *strong* evidence that internal strategies appear to be an effective aid in improving recall performance following relatively mild impairment, however the sustained effect of treatment is not known. There is strong evidence that internal strategies are not effective for those with severe.

Memory re-training programs

One RCT and three non-randomized studies explored the effectiveness of memory re-training programs to enhance memory following a brain injury. Ryan and Ruff [35], as explained above, randomly assigned patients into two groups: memory remediation (treatment group) and psychosocial treatment (control group) over a 6-week treatment period (4 days/week, 5.5 hours/day). No difference between groups was observed (both groups improved significantly over time), although when severity was considered it was observed that those with mild residual impairment benefited more from the treatment condition than the control condition (severely impaired continued to show no significant difference). Quemada et al. [38] treated 12 individuals with severe TBI during daily, 50-minute sessions over the period of 6 months using Wilson's Structural Behavioral Memory Program (a specified format utilizing behavioural compensation techniques, mnemonic strategies, environmental adaptations, and external memory aides). All patients achieved meaningful functional gains, however, improvements were generally not demonstrated on psychometric tests of memory functioning. Evans and Wilson [39] evaluated 4 patients with TBI in a group memory retraining intervention of two-hour weekly sessions for 11 months (consisted of reflections, memory exercises, games, strategy and coping discussions with emphasis on notebooks and diaries). Participants showed improvement in overall use of memory aides and in qualitative reductions of depression and anxiety. However, no significant improvements were noted on psychometric measures (Table VI).

Conclusions regarding memory re-training programs. Based on one RCT, there is *limited* evidence to suggest that memory-retraining programs are not effective for functional recovery. Memory re-training may be of benefit to those with mild impairment compared to severely impaired individuals at least in functional day-to-day memory. Performance on specific tests of memory may or may not change.

Executive function

Executive functioning refers to higher level cognitive functions that are primarily mediated by the frontal lobes and its connections throughout the brain. Executive functioning includes: insight, awareness, judgment, planning, organization, problem solving, multi-tasking and working memory [40]. The frontal lobes and subsequent subcortical connections tend to be one of the brain areas most likely to be injured following traumatic brain injury [41] and it is common for a TBI patient to present with cognitive and behavioural deficits in the absence of substantial physical impairment.

Younger brain injury patients (average age less than 40 years) tend to be most affected by executive functioning deficits, as younger patients are most desirous of returning to the community and pre-injury societal roles. Although those with executive dysfunction may be equipped to complete basic activities of daily living, certain instrumental activities such as banking, scheduling and household activities may not be possible due to the increased cognitive complexity of the tasks and reliance on a functional executive system. Younger individuals find the more advanced tasks such as driving and return to a competitive work environment to be the most relevant daily activities following brain injury [42].

Group interventions

Although executive function deficits are a common impairment for individuals, post-brain injury, there is little research addressing the impact of rehabilitation on increasing executive functioning capacity. It is possible that researchers and interventions aimed at improving community reintegration may in fact be focusing efforts on instrumental activities of daily living for which intact executive functions are necessary (Table VII).

Three non-RCTs examined the use of group intervention as a treatment for improving executive functioning following brain injury. Ownsworth et al. [43] assessed a 16-week support group program aimed to improve self-awareness and self-regulation skills. Following the 16-week intervention, there were significant improvements for self-regulation skills and level of psychosocial functioning, however, these results were not maintained at the 6-month follow-up.

Conclusions regarding group interventions. There is *limited* evidence that demonstrated the short-term effectiveness of group-based interventions for the treatment of executive dysfunction post brain injury

Table VI. The use of memory retraining programs to enhance memory.

Author/Year/Country/Design/PEDro/D&B	Eligibility criteria	Study methods	Outcome measures	Results
Ryan & Ruff 1988 [35] USA RCT D&B = 18 PEDro = 3	Inclusion: Time since injury between 1–7 years; medical documentation of serious head trauma; expressive and receptive language ability that allows for communication; one functional hand; visual acuity allowing for discrimination of letter and other stimuli; age between 16–65 years; motivation and availability for a 14-week period. Exclusion: Premorbid history of schizophrenic illness or other neuropsychiatric disturbance.	20 TBI patients divided into treatment and control groups according to score on Dementia Rating Scale (>133 mild, <134 moderate) received either attention and spatial integration exercise (experimental) or psychosocial treatment (control) over a 6 week treatment period (4 days/week, 5.5 hours/day).	The Benton Visual Retention Test (BVRT), Rey Osterieth Complex Figure Test (CFT), Taylor Complex Figure, Selective Reminding Test (SRT), Ruff Light Trail Learning Test (TLT), Wechsler Memory Scale logical memory subtest (WMS)	Both groups improved significantly over time ($p < 0.05$). The experimental group did not show significantly greater improvement when compared to control group (no p value reported). No significant differences between groups on any of the outcome measures. Subjects with mild neuropsychological impairments benefit more from memory remediation when compared to more severely impaired patients ($p < 0.001$).
Evans & Wilson 1992 [39] UK Single group intervention D&B = 10	Suffered brain injury with consequent impairment in memory functioning	Four ABI individuals and one stroke patient received a group intervention of 2 hr weekly sessions for 11 months of memory retraining consisting of reflections, memory exercises, games, strategy and coping discussions with special emphasis on use of notebooks and diaries.	Third party questionnaire on use of memory aids/strategies, Rivermead Behavioral Memory test (RBMT), and the Hospital Anxiety and Depression Scale (HAD) before, at 7 months and at the end of the group intervention.	The overall use of memory aids increased significantly between pre and midpoint intervention ($p < 0.05$) and pre-intervention and end of study ($p < 0.05$). RBMT scores did not improve. Group HAD scores not compared, but individual patients experienced qualitative reductions in depression and anxiety.
Quemada et al. 2003 [38] Spain Single group intervention D&B = 19	Inclusion: TBI causing memory impairment severe enough to interfere with autonomy in ADL; scores below the 40th percentile on both the California Verbal Learning Test (CVLT) and Rey Osterrieth Complex Figure Test (REY). Exclusion: IQ below 75 on the Wechsler Scale; presence of neuropsychiatric disorders; sensory deficits; history of substance abuse; previous neurological condition or learning disabilities.	12 severe TBI patients (GCS mean 5.7, PTA >28 days) with severe memory impairments received individualized treatment using Wilson's Structured Behavioral Memory Program in 50-minute sessions daily for 6 months.	Rey Osterrieth Complex Figure Test (REY), California Verbal Learning Test (CVLT), Rivermead Behavioural Memory Test (RBMT), and Memory Failures in Everyday memory questionnaire (MFE).	All patients achieved meaningful functional gains. Improvements were not found using REY, RBMT or MFE measures. There were some modest improvements in some scales of the CVLT (Total Words Correctly Recalled at the First Trial of the First List (AONE) $p = 0.03$), and Long Delay Free Recall Trial (LDFR) $p = 0.05$).

Table VI. Continued.

Author/Year/Country/ Design/PEDro/D&B	Eligibility criteria	Study methods	Outcome measures	Results
Hux et al. 2000 [60] USA Collection of case studies D&B = 8	Inclusion: Evidence of memory impairment, but not dependant on the profile of the impairment; hearing acuity adequate for conversational speech; visual acuity sufficient to allow for recognition of pictures of people; native speakers of American English. Exclusion: Aphasia; history of neurological problems other than TBI.	Seven male TBI patients were presented visual stimuli (photos of staff members) in individual sessions consisting of a probing and directed training activity (mnemonics & visual imagery) in varying frequencies (once per day, two times a week and five times a day)	Ability to name individuals in photographs.	Intervention was effective in 4/7 participants. Lower training frequencies were more effective than five times a day. The higher frequency resulted in longer encoding phases, and behavioral issues in some patients. No statistical comparisons made.

Table VII. The use of group therapy to enhance executive function.

Author/Year/Country/ Design/PEDro/D&B	Eligibility criteria	Study methods	Outcome measures	Results
Parente & Stapleton 1999 [61] Prospective controlled trial D&B = 12	Inclusion: Not specified Exclusion: Not specified	32 TBI patients with undefined etiologies participating in a group cognitive skills training module were compared to 64 matched controls who received similar services during the same time frame but who did not receive group training.	Success in training; Return to work; Job longevity	10 of 13 clients who completed the training program by the end of the year had maintained full employment for >60 days (76%) compared with 58% of the control group.
Parente et al. 1999 [62] USA Prospective controlled trial D&B = 10	Inclusion: Not specified Exclusion: Not specified	10 ABI patients were given tasks that trained working memory for 1 hour. Task included playing cards as outlined by Parente and Hermann (1996) requiring dual-processing, mental arithmetic, anagram solutions, serial logic tasks. Control clients matched to treatment group by sex and chronicity.	*Pre and post measures*: Digit Span Task (Forwards and Backwards); the Letter-number sequencing tasks from the WAIS-III.	No significant group differences in Digit Span test. Letter-number sequencing task WAIS-III differed significantly between groups pre/post treatment ($p < 0.05$).
Ownsworth et al. 2000 [43] Australia Single group intervention D&B = 20	Inclusion: Adequate cognitive skills to communicate; awareness of difficulties; motivation to produce changes in their lives. Exclusion: Substance abuse; psychiatric complications; severe cognitive impairment; individuals with challenging behaviours not shared by the others.	21 chronic ABI patients participated in a 16-week group support programme designed to improve self-awareness and regulation skills.	Changes in levels of self-awareness and self-regulation, changes emotional and behavioral problems, changes in psychosocial functioning pre, post and 6 months after treatment.	Post-assessment mean score for emotional and behavioural problems was significantly lower ($p < 0.001$), self-regulation skills improved significantly with no significant change in level of skills at 6-month follow-up, level of psychosocial functioning improved significantly ($p < 0.001$) with no significant change at 6-month follow-up.

(neurocognitive test performance does not necessarily change).

Goal management training

One RCT examined the efficacy of a Goal Management Program (GMP) in comparison to a Motor Skills Training group [44]. Participants in both groups improved, however those in the GMT group significantly improved on paper and pencil everyday tasks thought to be reliant on self-regulation (Table VIII).

Conclusions regarding goal management training. *Moderate* evidence, based on a single RCT, demonstrated that goal management training was effective for improving paper and pencil daily activities and preparation skills.

General cognitive rehabilitation

Interventions for treatment of cognitive deficits post brain injury tend to be diverse with variability between the interventions themselves and the outcome measures used to document results.

Cognitive rehabilitation strategies. Cicerone et al. [45] comprehensively reviewed cognitive rehabilitation and provided recommendations for clinical practice. As part of this review, comprehensive-holistic cognitive rehabilitation was endorsed as a therapy intervention following brain injury or stroke at the practice guideline level. This review was recently updated [3] spanning the literature from 1998–2002 (Table IX).

Along with the systematic reviews investigating cognitive rehabilitation strategies, 11 studies also explored issues surrounding the topic, including four RCTs.

In the studies by Dirette et al. [63], Rath et al. [64] and Cicerone et al. [45] comparisons of specific strategies using experimental techniques (randomized and non-randomized) are attempted. All groups demonstrated benefit from the interventions and in studies by Rath et al. [64] and Cicerone et al. [45] there were overall trends for improvement from the experimental groups. The study by Salazar et al. [46], provides contradictory results to these other studies in that no benefit was demonstrated for an intensive in-patient rehabilitation program versus a limited home based rehabilitation program. However, as highlighted by the authors of this study, their sample may not be representative of ABI in general as both groups demonstrated a very high rate of return to work (90% and 94%, respectively). When examining a subset of individuals who had more severe injuries a significant benefit from the cognitive rehabilitation program was observed.

Although there are differences in the delivery techniques of cognitive rehabilitation therapy, most studies demonstrated an overall improvement in cognitive abilities when considering within-group comparisons.

Conclusions regarding cognitive rehabilitation strategies. There is *limited* evidence that general cognitive rehabilitation therapy following brain injury is effective for improving cognition. Although there are variable strategies and protocols for cognitive rehabilitation, all comprehensive interventions appear to provide benefit.

Computer-assisted training

The use of computer-assisted cognitive retraining has multiple potential benefits within the rehabilitation setting post brain injury. Computer retraining allows for the flexibility in retraining procedures, increased individuality of therapy programs and also, decreases the amount of direct time a therapist is with the patient. There is also potential for continued cognitive retraining within the community setting (Table X).

Three non-RCTs examined the use of computer-assisted cognitive retraining for the purposes of general cognitive rehabilitation [47–49]. A review of this literature demonstrated that computer-assisted cognitive rehabilitation is not effective as an adjunct to the rehabilitation program.

Conclusions regarding computer-assisted training. There is *limited* evidence that computer-assisted cognitive retraining is not an effective adjunct to the rehabilitation program following a brain injury based on three non-randomized studies.

Pharmacological interventions

Pharmacological agents can assist with treating complications following brain injury including seizure disorders, pain and affective disorders. Medications have also been used to assist in controlling behaviours such as aggression and agitation after brain injury. It is possible that medications could impact cognition for patients with a brain injury. Therapy may be aimed at specific cognitive domains such as memory or attention, or may influence multiple cognitive domains since some medications are not necessarily selective for specific brain functions (Table XI).

Of four studies identified using pharmacological interventions, three studies used random assignment.

Table VIII. Goal management training in brain injury rehabilitation.

Author/Year/Country/ Design/PEDro/D&B	Eligibility criteria	Study methods	Outcome measures	Results
Levine et al. 2000 [44] Canada RCT D&B = 14 PEDro = 4	Inclusion: Not specified. Exclusion: Serious medical illness; psychiatric illness; substance abuse; refusal to participate; loss of contact over the 3 to 4 years; focal neurological syndromes or linguistic or mnestic disorders that would prevent participation in the training or completing the assessment measures.	30 ABI individuals were randomly assigned to receive brief trials of goal management training (GMT, $n = 15$) derived from Duncan's theory of goal neglect on disorganized behaviour following TBI or a Motor Skills Training (MST, $n = 15$). Training consisted of two one-hour sessions.	Proofreading; Grouping; Room Layout (designed by the author); Stroop Interference Procedure; Trail Making A and B; Digit Symbol subtest from the WAIS-R.	Although both groups improved, GMT was associated with significant gains on everyday paper-and-pencil tasks that mimic problematic tasks for patients with goal neglect (proofreading $p < 0.05$, grouping $p < 0.05$). GMT group was generally slower in the Stroop and Trail Making part B ($p < 0.05$, $p < 0.06$ respectively) reflecting increased care and attention compared with MST group.

Table IX. The use of cognitive rehabilitation strategies to enhance executive function.

Author/Year/Country/ Design/PEDro/D&B	Eligibility criteria	Study methods	Outcome measures	Results
Dirette et al. 1999 [63] USA RCT D&B = 16 PEDro = 4	Inclusion: No deficits in basic visual system; Fluency in English; Intact motor skills for completing typing tasks, familiar with basic computer keyboard use. Exclusion: Deficits in basic visual system.	30 participants were randomly assigned to the experimental or control condition. All participants received six, one-hour weekly session. The first week consisted of 45 minutes of participation in the pre-test and 15 minutes of participation in the weekly measures. Weeks 2–5 included 45 minutes of treatment and 15 minutes of participation in weekly measures. Those assigned to the control group received four 45-minute weekly sessions of remedial computer activities. Those assigned to the experimental group received four, 45-minute weekly sessions that included instruction in the use of three internal compensatory strategies for visual processing. During week six, participants attended a one-hour session that included 45 minutes of post-test data collection and 15 minutes of weekly measures.	*Everyday functional computer visual processing tasks* Accuracy and speed of completion of pre-test/post-test measures of ability to perform computer tasks requiring visual processing. Data entry tasks (Lotus program task and address typing task). *Computer measures of visual processing information*: Paced Auditory Serial Addition Task (PASAT) Matching Accuracy Test segments of the Brain Game program	Both groups (combined) improved significantly from pre-to-post test and on the weekly measures, however there were no significant differences between groups. No significant correlations were noted between motivation to participate and any of the pre-test to post-test or weekly skills. No significant influence of motivation was demonstrated on analysis of variance. According to self-reports, 80% of all participants used some type of compensatory strategy. The use of strategies appeared to increase performance on weekly measures and made gains less erratic.

Rath et al. 2003 [64] USA RCT D&B = 15 PEDro = 2	Inclusion: Met prescribed minimum "basic skills" criteria for inclusion in outpatient neuropsychological remediation groups; ability to sustain attention one-hour; take organized notes; receive feedback; state cognitive strength and weaknesses; adequate social skills; age between 20-65 years; ninth-grade education; English reading skills; impairments in social functioning. Exclusion: Psychoses; active substance abuse; other neurological conditions or severe lateralised deficits.	60 individuals with mild to severe TBI with a higher level of functioning were randomized into two groups: (1) patients received one individualized two-hour session each week for 24 weeks of a group treatment protocol (emotional self-regulation strategies, problem solving skills); or (2) a conventional neuropsychological rehabilitation program (control). 46 patients completed the intervention.	*Attention:* Weinberg Visual Cancellation test; Time and Error scores; Stroop Color-Word task; FAS-Controlled Oral Word Association test (FAS-COWAT); Will-Temperament Scale *Memory:* Wechsler Memory Scale (WMS III); Logical Memory Immediate and Delayed Recall; WMS III; Visual Reproduction Immediate and Delayed recall *Reasoning:* Watson-Glaser Critical Thinking Appraisal; Test 2+5 composite score; Wechsler Adult Intelligence Scale (WAIS-III); Comprehension subtest scaled score *Community integration:* Sickness Impact Profile (SIP); Recreation + Social Interaction Composite Score; Community Integration Questionnaire (CIQ) *Symptom Complaints:* Problem Checklist (PCL): Cognitive, Affective and Physical Severity scales; Brief Symptom Inventory (BSI): Depression, Anxiety and Hostility scales *Self-Esteem:* Rosenberg Self-Esteem scale (RSES) *Problem-solving:* Wisconsin Card Sorting test (WCST): Perseverative Response Score, Problem Solving Inventory (PSI), Self-appraised clear thinking and emotional self-regulation problem solving questionnaire (PSQ): Clear Thinking and Emotional Self-Regulation subscales, Problem Solving Roleplay test (PSRPT).	Treatment group showed significant improvements in problem solving and emotional self-regulation (PSQ), objective observer ratings of role-play scenarios (PSRPT), visual memory, self-esteem, fewer responses, gains in PSI total score ($p = 0.005$), PSQ Clear Thinking and Self-Regulation ($p = 0.01$ and $p < 0.05$), and PSRPT ($p < 0.005$). Control group showed significant improvements in the Watson-Glaser Critical Thinking test, somatic symptoms ($p < 0.005$), less severe cognitive symptoms after PCL, emotional self-regulation skills. Both the control and treatment groups improved on Logical Memory immediate recall, Logical Memory, Visual Memory delayed recall.

(*continued*)

Table IX. Continued.

Author/Year/Country/ Design/PEDro/D&B	Eligibility criteria	Study methods	Outcome measures	Results
Ruff et al. 1989 [65] USA RCT D&B = 19 PEDro = 5	Injured between 1–7 years earlier, serious head injury as suggested by medical documentation, sufficient expressive and receptive language ability for interpersonal communication, at least one functional hand, at least 25% intact visual fields, aged between 16–65 years, able to undergo 12-weeks of testing and treatment, no pre-morbid history of neuropsychiatric disturbance.	40 ABI subjects were randomized into groups comparing the efficacy of neuropsychological treatment (computer assisted selective attention, spatial integration, memory, and problem solving training modules) with a non-structured treatment providing equivalent professional attention and psychosocial support administered in daily sessions over an 8-week period.	Galvenston Orientation and Amnesia Test (GOAT); Dementia Rating Scale (DRS); Ruff Language Screening Examination (RLSE); Selective Reminding Test; Rey Complex Figure, 2 and 7 Test	Both groups showed significant improvement in neurological functioning. The experimental group achieved greater gains on measures of memory ($p = 0.03$) and error reduction ($p = 0.06$) for visual selective attention. Unexpected improvement in the treatment group's verbal IQ score ($p = 0.02$).
Salazar et al. 2000 [46] USA RCT D&B = 16 PEDro = 7	Inclusion: Moderate to severe closed head injury; head injury within 3 months of randomization; Rancho Los Amigos cognitive level of 7; Active duty military member; accompanied home setting with at least one responsible adult available to provide care; independent ambulation; no prior severe TBI that would preclude return to active duty following treatment. Exclusion: Mild TBI	120 active duty military personnel were randomly assigned to receive either: (1) in-hospital rehabilitation, or (2) home rehabilitation. The in-hospital rehabilitation treatment combined group and individual therapies, which were modified to fit military framework. A PT conducted the program. Patients were encouraged to follow military standards. The daily routine included physical fitness training and group and individual cognitive, speech, occupational and coping skills therapies. Specific group therapies were planning, organization, cognitive skills, pragmatic speech, milieu, psychotherapy, and community re-entry.	Return to work and fitness for military duty (at 1-year); Katz Adjustment Scale; Cognitive Behavioral Function Battery; Halstead- Reitan Neuropsychological Impairment Index	Return to work for the hospital group was 90% and 94% for the home group ($p = 0.51$). Fitness for military duty was 73% for the hospital group and 66% for the home group ($p = 0.43$). No significant differences were noted between groups on the Katz Adjustment scale. Although most patients showed an improvement in cognitive function within 1-year post-TBI, there was an increase in self-reported aggression in both groups. There were no significant differences between groups in verbal and visual memory or attention, or in general measures of cognitive or psychiatric function.

		Patients treated in the home rehabilitation group received TBI education and individual counseling from a psychiatric nurse. Educational materials were given to patients, along with recommended strategies for enhancing cognitive and organizational skills.		
Cicerone et al. 2004 [66] USA Prospective controlled trial D&B = 16	Included patients who were medically stable at admission, independent in basic self-care needs, cognitively able to participate in treatment, medically documented as TBI, >18 yrs of age, and had adequate language expression and comprehension Excluded patients with current substance use, psychiatric disturbance, and a family member who could not participate in the treatment, planning and support.	56 TBI patients received one of two treatment condidions: the treatment group received Intensive Cognitive Rehabilitation Program (ICRP) (*N*=27), while the control group received Standard Neurorehabilitation Program (SRP) (*N*=29)	Community Integration Questionnaire (CIQ) and Quality of CIQ (QCIQ) Neuropsychological functioning	Both groups significantly improved on the CIQ following treatment in favour of the ICRP group. ICRP group significantly improved with neuropsychological functioning after treatment. Participants with clinically significant improvements on the CIQ showed greater improvement on overall neuropsychological functioning.

(continued)

Table IX. Continued.

Author/Year/Country/ Design/PEDro/D&B	Eligibility criteria	Study methods	Outcome measures	Results
Rattok et al. 1992 [67] USA Prospective controlled trial D&B = 17	Inclusion: Diagnosis of TBI; at least one year post-injury; neurologically stable; unsuccessful vocational rehabilitation; age between 18-55; command of English; at least partial independence in basic activities of self-care; independence in ambulation; at least one functional hand and continence; a minimum IQ of 80; minimum demonstrated motivation for rehabilitation; intactness of a basic level of social appropriateness and manageability within a non-coercive) environment. Exclusion: History of past or present significant psychiatric complications; history of significant substance abuse; history of sociopathy; aphasic or dysarthric difficulties.	59 TBI patients for whom traditional treatment approaches had failed to stabilize personal and social adjustment were assigned to one of three treatment mixes: (1) balanced; (2) without individualized cognitive remediation; or (3) without small group interpersonal exercises. The treatments lasted for 20 consecutive weeks for five hours a day, four days a week.	*Psychometric measures:* Orientation Remedial Module (ORM); Purdue Pegboard; Figure recognition; Letter cancellation; Spatial relations; Navigations tasks; Vocabulary/comprehension/and spelling portions of the Metropolitan Achievement Test and the reading portion of the Wide Range Achievement Test; WAIS Verbal and Performance subtests; Recall errors on the Benton Visual Retention Test; Sentence Repetition portion of the Neurosensory Center Comprehensive Examination for Aphasia (NCCEA); Logical Memory subtest of the Wechsler Memory Scale (WMS); Category and shift portions of the RIRM similarities task; Category and shift portions of the RIRM object sorting task; Self generated portion of the RIRM telegram task; *Competence and independence:* Behavioural Competence Index (BCI); *Measures of intra- and interpersonal functioning:* Using four specially developed procedures; *Vocational outcome*: 10-point weighted scale.	Treatment mixes 1 and 3 (both received cognitive training) showed significant improvements (all $p < 0.05$) on the Purdue Pegboard, WAIS Block Design, RIRM similarities task, RIRM telegram task, verbal categorical reasoning (RIRM similarities task and RIRM telegram task), and visual processing(RIRMfigurerecognition task and RIRM letter cancellation task) whereas patients in treatment mix 2 did not. Vocational outcomes were statistically indistinguishable between groups.

Prigatano et al. 1987 [68] USA Retrospective controlled trial D&B = 15	Inclusion and exclusion not specified.	35 patients experiencing cognitive difficulties following severe closed-head-injury were separated into a neuropsychological rehabilitation (NRP) group and a control group. The NRP goal was to increase the patients' awareness and acceptance of their injury, residual deficits through intensive cognitive retraining and compensatory skills development.	Verbal IQ; Performance IQ Vocabulary; Block Design and Digit Symbol subtests of the Wechsler Adult Intelligence Scale (WAIS-R); Memory Quotient, Logical Memory and Visual Reproduction subtests of the Wechsler Memory Scale; Trail Making Test; Finger Tapping Test and Tactual Performance Test of the Halstead Reitan Neuropsychological test Battery; Russell-Neurenger Average Impairment Rating (AIR). KATZ Adjustment Scale Relatives Form; Vocational status.	NRP treatment group had significantly better improvements than the control group on WAIS Performance IQ and Block Design Scale, as well as the Wechsler Memory Quotient. The control group performed significantly better than treatment group on the Tactual Performance Test with dominant hand ($p = 0.03$). No other differences observed between groups in neuropsychological measures. At follow up, 50% of the patients in the NRP groups were gainfully employed or in school compared with only 29% of those patients in the control group.
Ben-Yishay et al. 1987 [69] USA Single group intervention D&B = 11	Inclusion: 18–55 years of age; verbal or performance IQ > 80; Ambulatory capability manageable without physical restraints; Able to reliably engage in two-way verbal communication; Deemed unemployed or unable to pursue academic studies in any capacity at program entry. Exclusion: History of previous brain injury; significant psychiatric history; significant substance abuse.	94 TBI patients participated in a two-phase outpatient day program involving intensive, systematic, holistic remedial interventions (Phase 1: 20 weeks, 5 h/day, 4 days/week) and individualized, guided occupational trails culminating in a vocational placement (Phase 2: 3–9 months).	Employability Rating Scale	At the end of phase 2, 84% of previously unemployable patients had attained the ability to engage in productive endeavors. Over three years, a tendency emerged for the number of patients employed at a competitive level to decrease.
Laatsch et al. 1999 [70] USA Single group intervention D&B = 8	TBI following motor vehicle accidents and fit criteria of mild to moderate severity (GCS 11–15), age between 18–65 years	Five TBI patients received individualized cognitive rehabilitation sessions. An optimal individualized cognitive rehabilitation therapy (CRT) was designed for each patient based on results of the Neuropsychological battery of tests and SPECT imagining.	*Neuropsychological battery:* Wechsler Adult Intelligence Scale-revised, Wechsler Memory Scale-revised, California Verbal Learning Test, Rey Complex Figure Test, Stroop Colour-Word Test, Wisconsin Card Sorting Test. SPECT Imagining was also administered. All measures administered prior to, at completion and 3–12 months post-treatment.	CRT was found to be effective in improving both neuropsychological and everyday functioning. All patients were able to be more productive in their lives following treatment. No statistical comparisons reported.

(*continued*)

Table IX. Continued.

Author/Year/Country/ Design/PEDro/D&B	Eligibility criteria	Study methods	Outcome measures	Results
Harrington & Levandowski 1987 [71] USA Single group intervention D&B = 15	Enrolled in a community college head injury recovery program, confirmed neurological diagnoses made by qualified physician, diagnoses confirmed through one or more of the following methods: neurological examination, arteriogram, EEG, brain scans, pneumo-encephalograms, X-rays, and surgery.	18 TBI adults received a two- year, structured retraining program consisting of five sequential modules (orientation, perceptual-cognitive processing, perceptual-cognitive integration, logical reasoning and problem solving and transitional community module, including work experience) in a neurodevelopmental hierarchy.	All 269 items of the Luria-Nebraska Neuropsychological Battery (LNNB) This battery was administered before and after training.	Significant improvements on all LNNB clinical scales except tactile scale. The visual scale was the most frequently improved, along with reading, math, memory and motor skills.
Brett & Laatsch 1998 [72] USA Single group intervention D&B = 12	High school attendance and intelligence in the borderline range or above as previously determined by the school system.	10 TBI high school students participated in an individualized, bi-weekly session (40 minutes) for 6 months of computer administered Rehabilitation Therapy (CRT) based on a 3 level developmental model of cognitive rehabilitation: *Level 1*: alertness, attention and concentration, *Level 2*: perception and memory, *Level 3*: executive processes (problem solving).	All measures assessed pre- and post-treatment. Test of Nonverbal intelligence 2 (TONI-2), Culture-Free Self Esteem Inventories 2nd edition (CFSEI-2), Benton Visual Form Discrimination Test, Multilingual Aphasia Examination (MAE) Token Test, Stroop Colour and Word Test, Wechsler Intelligence Scale for Children III (WISC-III), Freedom from Distractibility Scale, Picture Completion Subtest, Wide Range Assessment of Memory and Learning (WRAML) Screening Subtests: Picture Memory, Design Memory, Verbal Learning, Story Memory, Tower of London, Wisconsin Card Sorting Test	Significant improvements in memory skills (WRAML screen: $p = 0.025$); no significant differences found in any other measure.

Table X. The use of computer assisted training to enhance executive function.

Author/Year/Country/ Design/PEDro/D&B	Eligibility criteria	Study methods	Outcome measures	Results
Middleton et al. 1991 [49] USA Prospective controlled trial D&B = 12	Inclusion: Not reported Exclusion: Not reported	36 patients received 96 hours of educational training focusing on improving attention, concentration, perceptual skills, and problem solving. Each patient received an additional 32 hours of computer-assisted treatment. Treatment period lasted 8 weeks. The attention and memory software included seven separate programs presented to patients in the following order: Visual Tracking, Visual Reaction with Multiple Stimuli, Simultaneous Multiple Attention, Visual Memory, Spatial Memory, Paired Associates, Recognition Recall. The Reasoning and Logical thinking software included seven separate programs presented in the following order: number manipulations, checker exchange, King's Rule, Gnee or Not gnee, High Wire Logic, Knight's Challenge, Deduction.	*Standard neuropsychological assessment*: (1) *Attention and Memory:* Digit Span subtest of WAIS-R, Paired-associates subtest of the Wechsler Memory Scale, Knox's Cube (2) *Measures of Reasoning*: Concept Formation subtest of the Woodcock- Johnson Psychoeducational Battery, Abstraction subtest of the Shipley Inistitute of Living Scale, Block counting.	Significant improvements in cognitive functioning within each group following treatment. Performance on test of attention and memory (WAIS-R Digit Span, Wechsler Paired Associates, Knox's Cube) improved on average by 12% while reasoning performance improved on average of 16%. No differential effects associated with treatment group were observed for either the attention and memory test or the reasoning test. Gains made by both groups were similar on all measures.
Chen et al. 1997 [47] USA Retrospective controlled trial D&B = 12	Included patients who sustained a CHI and were treated b/w 1983 and 1991 at the Neuroscience Center of Indianapolis, ≥18 years, ≥9 years of education, and had neuropsychological evaluations before and after computer-assisted cognitive rehabilitation (CACR) within a period of 4 months. Exclusion not specified.	20 closed-head-injured (CHI) patients who received hierarchically based CACR following inpatient neurorehabilitation were compared to 20 matched CHI controls who received various other therapies including speech therapy and occupational therapy.	Pre- and Post-neuropsychological test scores (attention, visual spatial ability, memory and problem solving)	CACR and the comparison group showed significant post-treatment gains on the neuropsychological test scores, with the CACR group making gains on 15 measures, and the control group making gains on 7 measures. There were, however, no significant differences between the groups on their post-treatment gains.

(*continued*)

Table X. Continued.

Author/Year/Country/ Design/PEDro/D&B	Eligibility criteria	Study methods	Outcome measures	Results
Ruff et al. 1994 [48] USA Single group intervention D&B = 16	Inclusion: Between ages 16–50; Severe head injury documented in medical records; No evidence of severe disorientation or confusion at time of entry; at least 6 months post-injury; Dementia Rating Scale; Ruff Language Screening Examination; Sufficient vision to select stimuli on computerized screen; At least one functional hand required for manual dexterity to interact with demands of the computer program (assessed with computer screening tasks); No reported premorbid history of psychiatric disorders resulting in hospitalization; No premorbid neurological disorders; No substance abuse since injury. Exclusion: None specified	15 patients were randomly assigned to one of two treatment conditions: (1) patients received the attention training first, followed by memory training; or (2) patients received memory training, followed by attention training.	Computer-based assessments with THINKable- type exercises (attention and memory tasks used percentage of correct responses for total attempts made). *Neuropsychological tests*: 2+7 Selective Attention Test, WAIS-R Digit Symbol, Continuous Performance Test (CPT) *Memory*: Rey Auditory verbal Learning Test, Corsi Block Learning Test. Behavioral assessment included a questionnaire filled out by subjects. Pre- and post- treatment assessment including memory subsets of the Wechsler Memory Scale and the Beck Depression Scale.	THINKable computer-based attention training results in significant improvements ($p = 0.003$). Significant improvements in Memory II, none demonstrated in Memory I or III. No improvements on the 2+7 Selective Attention Test, Significant improvements in digit symbol scores, No significant changes in the CPT score for both conditions. Gains made in memory measures were significant for the Rey Verbal Learning total and Corsi Block Learning total, however no significant gains were made on the gains of either condition. Patient ratings were consistently higher than observer ratings on both the attention and memory-based behaviours. No difference shown over time on patient attention ratings, however objective ratings (family or friend) suggest significant changes. Differences noted in both patient and observer memory ratings. Significant improvements made on the part III (mental control subsection) and part IV (logical memory) of the Wechsler Memory Scale. All other sections of Wechsler failed to reach significance.

Table XI. Pharmacologic interventions and cognitive functioning.

Author/Year/Country/ Design/PEDro/D&B	Eligibility criteria	Study methods	Outcome measures	Results
McDowell et al. 1998 [50] USA RCT PEDro = 4 D&B = 18	Inclusion: Not specified. Exclusion: Dementia (MMSE < 26); deficits in oculomotor; uncorrected acuity or visual field; a major mental illness; uncontrolled high blood pressure; pregnancy; or current use of centrally acting mechanisms.	24 patients participated in a double blind, crossover design. Patients were randomly assigned to one of two groups: (1) Administration of bromocriptine, followed by treatment with placebo; or (2) the reverse order of administration. The dose of bromocriptine was 2.5 mg	Bi-letter cancellation task, Dual Task Paradigm, Stroop test, Spatial delayed-response task, Wisconsin card sorting test (WCST), Verbal span test, Trail-making test (TMT).	Bromocriptine had a significant effect on the dual-task, TMT, the Stroop Test, WCST and FAS Bromocriptine had no significant effect on working memory tasks.
Speech et al. 1993 [51] USA RCT D&B = 18 PEDro = 7	Inclusion: More than 20 years of age; high school graduate; No history of learning problems, special education assistance or ADHD; No history of treatment for neurological or psychiatric disorders including additional head injuries. Exclusion: Not specified.	A double blind crossover study design was used. 12 patients were randomly assigned to receive one of two treatment conditions: (1) 0.3 mg/kg b.i.d. (8a, and 12 pm) of methylphenidate for one week, followed by one week of placebo; or (2) the reverse order of the administration.	*Attention* Gordon Diagnostic System; Digit Symbol and Digit Span subtests of WAIS-R *Cognitive Processing Speed*: Stroop Interference Test; Sternberg High Speed Scanning Task *Learning*: Selective Reminding Test; Serial Digit Test *Social Personality Functioning*: Katz Adjustment Scale (KAS)	No significant differences were noted between drug and placebo conditions on any of the neurobehavioral outcome measures.
Alvarez et al. 2003 [53] Spain Single group intervention D&B = 15	Inclusion and exclusion criteria not specified.	20 patients were used to determine potential effects of repeated injections of the Cerebrolysin solution (30 mg/day) on brain bioelectrical activity and on cognitive performance in post-acute TBI patients. The treatment lasted a period of four weeks (20 infusions).	Syndrome Kurztest (SKT); Brain bioelectrical activity using EEG spectral analysis and topographic mapping.	Following treatment, patients showed a significant decrease in slow brain bioelectrical activity frequencies delta ($p < 0.01$) and theta ($p < 0.05$), significantly enhanced relative beta activity power ($p < 0.01$) and a non-significant increase in average alpha activity after treatment in comparison with baseline. EEG power ratio scores were significantly reduced ($p < 0.01$). Significant improvements were demonstrated in SKT cognitive performance ($p < 0.01$). SKT scores decreased significantly compared with baseline after treatment, but not three months later ($p < 0.05$). Significant improvements in GOS scores were noted ($p < 0.05$).

All four studies used different pharmacological agents in determining the efficacy of intervention. McDowell et al. [50] compared the use of Bromocriptine with a placebo and found significant improvements for the drug treatment group on measures of executive function and in dual-task performance, but not measures that are thought to reflect working memory.

Speech et al. [51] examined the effects of Methylphenidate and found no significant differences between treatment and controls on measures of attention, cognitive processing speed, learning and social personality functioning. Schneider et al. [52] randomly assigned patients to receive Amantadine or placebo. There was a general trend towards improvements on cognitive rehabilitation and behavioural functioning, but there were no significant differences between groups. Alvarez et al. [53] explored the use of Cerebrolysin, a neuropeptide preparation, which has been demonstrated to have a neuroprotective and neurotrophic effect. A brief neuropsychological battery (SKT) was administered and for the nine patients able to participate using this test significant improvements were noted.

Conclusions regarding pharmacological interventions. Pharmacological agents have potential for improving the cognitive functioning of an individual following a brain injury. As with other rehabilitation interventions, the need to provide controls and to take into account spontaneous recovery is essential to clarify if medications do have a specific beneficial effect. Based on one RCT, there is *moderate* evidence that Bromocriptine helps to improve executive functioning after a single dose administration following brain injury. There is *moderate* evidence that Methylphenidate does not improve overall cognitive functioning based on one randomized trial (however, as discussed earlier there is strong evidence that MP has a beneficial effect on attention). There is *limited* evidence to suggest that Cerebrolysin has the potential to improve outcome and cognitive function post brain injury. It is suggested that controlled trials will be necessary to evaluate this drug further. There is *moderate* evidence that Amantadine is not effective for improving overall cognitive function based on the results of one RCT.

Exercise intervention

The association between exercise and improvements in cognitive functioning are not immediately evident, however, animal model studies have found that exercise can positively affect cognition. One retrospective controlled trial [54] investigated the notion that exercise could benefit cognitive functioning with 13 individuals with brain injury. A stationary bicycle in conjunction with non-immersive virtual reality was administered over a period of four weeks. The intervention group performed significantly better than the control group on Digit Symbol, and verbal and visual learning tasks. Reaction and movement times improved significantly after a single virtual reality session (Table XII).

Conclusions regarding exercise interventions. Limited evidence demonstrated that exercise interventions have a positive impact on visual and verbal learning following brain injury.

Discussion of cognitive interventions

Based on a systematic review of the literature examining cognitive intervention following moderate to severe acquired brain injury, 64 studies were evaluated (although not all studies were explicitly discussed in this article). Areas reviewed included attention/concentration (11 studies), learning and memory (30 studies), executive functioning (four studies), and general cognitive rehabilitation approaches (19 studies).

This review supported the observation that cognitive rehabilitation is an effective intervention following acquired brain injury and is in agreement with other published reviews [2, 3, 45]. Cicerone et al. [3, 45] comprehensively reviewed cognitive rehabilitation of persons with traumatic brain injury (TBI) and stroke. Based on the literature reviewed, recommendations of practice standards, practice guidelines, and practice options were made. Of relevance to brain injury, several recommendations were made:

- Specific interventions for functional communication deficits, including pragmatic conversational skills were recommended for persons with TBI;
- For persons with mild memory impairments following brain injury, memory strategy training, including the use of internal aids such as visual imagery and external compensatory strategies such as using a diary or planner, was recommended;
- During the post-acute phase following brain injury, strategy training for attention deficits was recommended for persons with TBI.

In this article, we did not address language functioning or cognitive-communication as it was addressed in a separate chapter (ERABI).

Table XII. The effect of exercise and conditioning on cognition.

Author/Year/Country/ Design/PEDro/D&B	Eligibility criteria	Study methods	Outcome measures	Results
Grealy et al. 1999 [54] Scotland Retrospective controlled trial D&B = 15	Inclusion: Ambulatory; good sitting balance; no perceptual disabilities that would prevent view of monitor; passed medical exam to ensure suitability for exercise. Exclusion: Patients were excluded if they were unable to score on the Digit Span or Digit Symbol (WAIS-R); unable to carry out simple instructions, or those with insufficient language skills to allow their verbal learning capacity to be assessed.	The experimental group consisted of 13 brain-injured patients who took part in a non-immersive virtual reality exercise. The information of 320 patients was collected and acted as the control group.	*Attention*: Digit Span (forward and backward) Digit Symbol (WAIS-R) Trails A and B. *Learning and Memory*: Auditory Verbal Learning (Rey), Visual Learning (AMIPB), Logical Memory (AMIPB), Complex figure (Rey) tests.	Following the four-week intervention, patients performed significantly better than controls on digit symbol ($p < 0.01$), verbal ($p < 0.05$), and visual learning tasks ($p < 0.01$). Significant improvements in reaction time ($p < 0.01$) and movement times ($p < 0.05$) were observed following a single round of virtual reality training.

The review supported the use of internal and external memory strategies, as well as memory training programs with various caveats attached to the recommendations (e.g., differential effect of mild vs severe impairment, functional memory vs psychometric measures of memory, etc).

Strong evidence was found for pharmacological intervention in improving attention (primarily speed of processing), particularly for Methylphenidate. Of the studies reviewed, computerized training programs used to enhance attention do not appear effective when compared to other non-specific 'remediation' sessions. However, dual-task training appears to be effective in improving speed of processing, particularly when incorporating training in self-management strategies.

Although executive deficits are prominent in the area of brain injury (particularly traumatic brain injury), and often result in the greatest impairment for re-integration back into the community very few studies have specifically evaluated the effects of treatment within this domain. Of those studies evaluated within this review, moderate-to-limited evidence was found for group intervention and goal-management training. Some evidence for pharmacological intervention was also supported.

Gordon et al. [2] systematically reviewed traumatic brain injury rehabilitation. The review is comprehensive and covers all aspects of recovery and rehabilitation from acute hospitalization to community reintegration, including the physical, cognitive and emotional/psychiatric aspects of traumatic brain injury. Differences between Gordon et al. [2] review and the current review is that they used the American Academy of Neurology classes of evidence (I–IV), largely excluded studies that had a sample size less than 20 for TBI and control groups, and included mild, moderate and severe TBI. Regardless, conclusions drawn remain remarkably similar to the current review.

Analysis of findings from the current review as well as those from Cicerone et al. [3, 45] and Gordon et al. [2] all suggest that future studies need to control for patient characteristics (e.g., level of impairment needs to be clearly defined, not just severity of injury), spontaneous recovery and practice effects on outcome measures used. Studies should not just rely on psychometric tests but should consider functional outcome measures and long-term effects of treatment interventions should be monitored through follow-up.

Acknowledgements

This work was supported by the Ontario Neurotrauama Foundation.

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