6. Interventions for Cognition and Cognitive-Communication Post Acquired Brain Injury

Shawn Marshall MD MSc
Penny Welch-West (M.Cl.Sc. SLP)
Connie Ferri (MSc. SLP)
Pavlina Faltynek MSc
Shannon Janzen MSc
Leanne Togher PhD,
Robert Teasell MD

Key Points

Drill and practice training may not be effective for the remediation of attention following an ABI.

Dual-task training has been shown to improve measures of attention to the extent that the ABI population does not significantly differ from healthy controls, however it is undetermined if the strength of these effects compared to non-dual-task training are greater.

Computer-based interventions are no more effective than no intervention in improving measures of attention and concentration post ABI.

Repetitive virtual reality tasks which include repetition are effective in improving attention and concentration in ABI populations.

Goal management training is effective in assisting those who sustain an ABI learning to manage life goals through improved attention.

In general, a variety of non-specific attentional training programs appear to be effective for improving attentional scores following an ABI.

The addition of a therapy animal to an attentional training program may enhance concentration gains.

Therapies which focus on emotional regulation do not appear to be effective at improving attention post ABI, while mindfulness may improve some areas.

In order to determine if attentional training is effective in improving attention post-ABI standardized protocols must be developed to allow between study comparisons.

Tasks that involve mathematical skills may be effective at improving attention post ABI.

Transcranial direct current stimulation may be effective in remediating attentional deficits when combined with computer assisted training in ABI populations.

Repeated magnetic transcranial stimulation may be effective in remediating attentional deficits following an ABI.

It is unclear as to whether donepezil may improve attention in individuals with a moderate to severe ABI.
The effectiveness of methylphenidate treatment to improve cognitive function following brain injury is unclear.

Methylphenidate may be effective in improving reaction time for working memory.

Response to methylphenidate may depend on the presence of the Met genotype.

Bromocriptine does not appear to improve attention in those with an ABI.

Cerebrolysin may be beneficial for improving clinical outcomes and cognitive functioning following brain injury; however, controlled trials are needed to further evaluate its efficacy.

Rivastigmine may not be effective in treating attention deficits post ABI.

Amantadine may not be effective in treating attention deficits following an ABI.

Hyperbaric oxygen therapy may improve attention and processing speed following an ABI; however more prospective data is required in order to make a conclusion.

Dextroamphetamine may not be an effective treatment for attentional deficits following an ABI and may actually increase agitation.

Pager and voice-organizer programs may improve a patient's ability to complete tasks post TBI.

Personal digital assistant (PDA) devices are superior to paper-based interventions at improving memory and task completion post TBI; specially when introduced using systematic instructions and in combination with occupational therapy. Patients who have used previous memory aids might benefit from this intervention the most.

Text message prompts sent to a patient's smartphone, when used alone or in combination with other memory-improvement therapies, likely improve task completion post TBI. However, risk exists of device dependency exists.

A television assisted prompting (TAP) program may be superior to other methods of memory prompting in post TBI patients.

Automated prompting systems, such as Guide (audio-verbal interactive micro-prompting system) and a computerized tracking system, can reduce the number of prompts needed from support staff to patients to complete tasks post TBI.
Calendars may be effective tools for improving memory and task completion post ABI.

The use of a diary may help to improve memory and task completion post ABI.

Virtual reality programs may enhance the recovery of memory, learning, but there is currently limited evidence supporting the use of virtual reality programs. The evidence is unclear as to which specific programs benefit memory rehabilitation and whether or not they are superior to manual training therapies.

Internal strategies such as self-imagination, spaced retrieval and rehearsal, and multiple encoding are effective for improving memory following an ABI.

Memory-retraining programs appear effective, particularly for functional recovery although performance on specific tests of memory may or may not change.

Some specific computer-based software seem to be effective for improving memory post ABI.

Computer-based interventions may be as effective as therapist administered interventions.

Emotional self-regulation therapy may be effective for improving specific elements of memory.

Attention training programs may not be effective for improving memory, but memory training programs are.

Interventions which include multiple learning techniques such as modelling, observation, verbal instruction, etc. are more effective than interventions which include a singular learning method.

Cranial electrotherapy stimulation may not be effective at enhancing memory and recall abilities following TBI.

Donepezil likely improves memory following TBI.

Methylphenidate likely does not improve memory or learning following an ABI.

Sertraline has not been shown to improve learning, or memory within the first 12 months post TBI, and may be associated with side effects.

Amantadine is not effective for improving learning and memory deficits post ABI.

Pramiracetam might improve memory in males post TBI; however, additional studies are required.

Physostigmine may improve long-term memory in men with TBI, however more studies are required.

More studies are required to determine if the positive effects of bromocriptine on verbal memory seen so far are of potential value.

Cerebrolysin may be beneficial for the improvement of clinical outcome and cognitive functioning following brain injury; however, controlled trials are needed to further evaluate its efficacy.

The administration of growth hormone complexes likely does not improve learning and memory following an ABI.

Rivastigmine is not effective in treating memory deficits post ABI.

Hyperbaric oxygen therapy may be promising for improving memory following an ABI; however, more controlled studies are required.

Targeted hypnosis may improve memory, attention, and cognitive function in post TBI patients or stroke; however, only as long as the intervention is being administered.

Attention training programs likely do not improve executive functioning.

General cognitive training programs which include problem-solving appear to be effective for improving executive functioning following an ABI.

Virtual reality does not likely improve executive functioning following an ABI.

Computer or smartphone software programs (BrainHQ, Parrot Software, ProSolv app) may not be superior to common interventions at improving memory, attention, and problem-solving skills in patients post TBI.

Goal management training may be superior to motor skills training at improving everyday skills (meal preparation), but not intelligence or neuropsychological outcomes in patients post TBI.

Heart rate variability biofeedback may improve executive functions; however, more controlled studies are required to make further conclusions.

Group goal-oriented interventions are effective for the remediation of executive functions, including comprehension and problem solving.

Emotional regulation interventions delivered in a group setting may improve executive function in patients post TBI; however, it is unclear if it is superior at doing so compared to conventional cognitive remediation.

The SMART program appears to be effective for improving executive functioning following an ABI.

Touch screen-based games which include components of metacognition may be effective for improving self-awareness.

Metacognitive instruction does not appear to improve comprehension or abstract reasoning; however, more studies are needed to fully evaluate its effects.

General cognitive rehabilitation programs are effective for improving cognitive functioning following an ABI.

There is limited evidence that mindfulness based stress reduction is effective for improving cognitive functioning.

Corrective video feedback is more effective than verbal feedback alone for improving general cognitive function and self-awareness.

Remedial and adaptive occupational therapy are equally effective for improving general cognitive functioning.

Donepezil might improve attention, learning and short-term memory following TBI; however, side effects may incur from its use.

The effectiveness of methylphenidate to improve cognitive impairment following brain injury is unclear. Further studies with larger populations are required.

Sertraline has not been shown to improve cognitive functioning within the first 12 months post TBI and may be associated with side effects.
Amantadine is not effective at improving generalized cognition. Its impact on executive functioning should be studied further.

Bromocriptine may improve other measures of cognition such as attention, but its effects on generalized cognition are conflicting. More research is required.

The administration of human growth hormones appears to have positive (although sometimes limited effects) on general and executive functioning in those with an ABI.

Rivastigmine is not effective in treating general or executive dysfunction post ABI.

Hyperbaric oxygen therapy may be beneficial for improving general and executive functioning following an ABI; however, more research is needed.

Dextroamphetamine is moderate evidence to suggest that dextroamphetamine is not effective for the remediation of general functioning.

Communicating "yes/no" responses with consistent training and environmental enrichments does not improve communication responses in individuals post ABI.

Retrieval practice is effective for improving verbal communication in individuals with an ABI.

Targeted figurative language therapy improves communication and comprehension in individuals with TBI; although the severity of the injury may moderate these effects.

Text-to-speech technology improves reading rates in individuals with TBI, but not comprehension.
Training in social skills, social communication or pragmatics is effective in improving communication following brain injury.

Goal-driven interventions may be effective in improving social communication skills and goals following TBI.

Group Interactive Structured Treatment (GIST) is effective for improving social communication skills following an ABI.

Computer-based game programs which deliver cognitive-communication skills training may be effective for improving social skills.

Providing communication training to individuals who interact with people with TBI is effective and encourages two-way dialogue.

Providing training to the communication partner and the individual with TBI together is more effective than training the individual with TBI alone.

Facial affect recognition and emotional interference training improves emotional perception post ABI.

Short intervention designed to improve emotional prosody is not effective post ABI.

Cognitive Pragmatic Treatment (CPT) program is effective at improving comprehension and production of a communication act.

The Treatment for Impairments in Social Cognition and Emotion Regulation and Cogniplus protocols are effective for improving emotional processing and emotional intelligence in individuals with an ABI.

Table of Contents

6.0 Introduction 1

6.1 Rehabilitation of Attention, Concentration, and Information Processing Speed 3

6.1.1 Non-Pharmacological Interventions 3

6.1.1.1 Drill and Practice 3

6.1.1.2 Dual-Task Training 5

6.1.1.3 Technological Interventions 7

6.1.1.4 Attention Training Programs 12

6.1.1.5 Brain Stimulation Techniques 21

6.1.2 Pharmacological Interventions 23

6.1.2.1 Donepezil 23

6.1.2.2 Methylphenidate 25

6.1.2.3 Bromocriptine 29

6.1.2.4 Cerebrolysin 31

6.1.2.5 Rivastigmine 32

6.1.2.6 Amantadine 33

6.1.2.7 Hyperbaric oxygen therapy 34

6.1.2.8 Dextroamphetamine 35

6.2 Rehabilitation of Learning and Memory Deficits 36

6.2.1 Non-Pharmacological Interventions 37

6.2.1.1 Assistive Devices 37

6.2.1.1.1 External Technology Aids 37

6.2.1.1.2 Internal Memory Strategies 50

6.2.1.2 Learning and Memory Training Programs 58

6.2.1.3 Cranial Electrotherapy Stimulation 77

6.2.2 Pharmacological Interventions 78

6.2.2.1 Donepezil 78

6.2.2.2 Methylphenidate 81

6.2.2.3 Sertraline 83

6.2.2.4 Amantadine 84

6.2.2.5 Pramiracetam 85

6.2.2.6 Physostigmine 86

6.2.2.7 Bromocriptine 88

6.2.2.8 Cerebrolysin 89

6.2.2.9 Growth Hormone (GH) Replacement Therapy *90*
6.2.2.10 Rivastigmine *92*
6.2.2.11 Hyberbaric oxygen therapy *93*
6.3 Rehabilitation of Problem Solving, Executive and General Cognitive Functioning 94
6.3.1 Non-Pharmacological Interventions 95
6.3.1.1 Rehabilitation of Executive Functioning *95*
6.3.1.2 Rehabilitation of General Cognitive Functioning *112*
6.3.2 Pharmacological Interventions 116
6.3.2.1 Donepezil *116*
6.3.2.2 Methylphenidate *117*
6.3.2.3 Sertraline *119*
6.3.2.4 Amantadine *120*
6.3.2.5 Bromocriptine *122*
6.3.2.6 Growth Hormone (GH) Replacement Therapy *124*
6.3.2.7 Rivastigmine *126*
6.3.2.8 Hyberbaric Oxygen Therapy *127*
6.3.2.9 Dextroamphetamine *128*
6.4 Verbal and Written Communication 129
6.4.1 Remediation of Verbal and Written Communication 129
6.5 Social Communication Skills Training for Individuals and Communication Partners 133
6.5.1 Social Communication Skills Training 133
6.5.2 Training Communication Partners 137
6.5.3 Non-Verbal Communication 141
6.5.3.1 Emotional Intelligence *141*
6.5.4 Alternative and Augmentative Communication 145
6.5.4.1 Organizational Word Retrieval Strategies: *146*
6.5.4.2 Non-Electronic Communication Board: *146*
6.5.4.3 Eye-Gaze Communication Board: *146*
6.5.4.4 Bliss Symbols: *147*
6.5.4.5 Pictograms: *147*
6.5.4.6 Picture/Symbol Based Boards: *147*
6.5.4.7 Alphabet Boards: *147*
6.5.4.8 Memory Aids *148*
6.5.4.9 Synthetic Voice: *148*
6.5.4.10 Sign Language: *148*

6.6 Conclusions **148**
6.7 Summary **150**
6.8 References **160**

Marshall S, Welch-West P, Ferri C, Faltynek P, Janzen S, Togher L, Teasell R. (2019). Interventions for Cognition and Cognitive-Communication Post Acquired Brain Injury. In Teasell R, Cullen N, Marshall S, Janzen S, Faltynek P, Bayley M, editors. Evidence-Based Review of Moderate to Severe Acquired Brain Injury. Version 13.0: p1-175.

Abbreviations

ABI	Acquired Brain Injury
APT	Attention Process Training
CES	Cranial Electrotherapy Stimulation
GH	Growth Hormone
Met	Methionine Allele
PASAT	Paced Auditory Serial Addition Task
PDA	Personal Digital Assistant
PTA	Post Traumatic Amnesia
RCT	Randomized Controlled Trial
TBI	Traumatic Brain Injury
TPM	Time Pressure Management
Val	Valine Allele

Interventions for Cognition and Cognitive-Communication Post Acquired Brain Injury

6.0 Introduction

Cognitive and cognitive-communication deficits are common sequelae of acquired brain injury (ABI) which can negatively affect many areas of cognition such as attention, memory, reasoning, problem solving and executive function, as well as areas of communication including verbal expression, auditory comprehension, reading, written expression and social communication skills. Each of these cognitive functions represents a unique area of cognition and communication that allows individuals to execute activities of daily living, which may include work, play, school and social exchange. Cognitive impairment can be caused not only by the initial trauma, but also by secondary inflammation or insult. Compared to mild traumatic brain injury (TBI), moderate/severe TBI is associated with more severe and persistent deficits, with about 65% of patients reporting long-term cognitive problems (Rabinowitz & Levin, 2014). The effects of TBI on overall cognitive and cognitive-communication functioning vary depending on time post injury (Schretlen & Shapiro, 2003). Even with good medical prognosis, both cognitive and cognitive-communication ability remain one of the best predictors of successful return to work and independent living (Zasler ND, 2013). Due to the complex nature of the brain, there are a multitude of ways that each trauma may impact cognition and cognitive-communication. As a result, there are a variety of interventions available to clinicians to help rehabilitate these deficits post ABI.

In the broadest sense, interventions may be classified as pharmacological and non-pharmacological. Pharmacological interventions use medication to remediate deficits. These types of medications usually moderate neurotransmitters in the brain that regulate cognitive functions. By influencing the concentration and absorption of either excitatory or inhibitory neurotransmitters these medications are able to influence functions such as memory, attention, and social behaviours among others (Zasler ND, 2013). Non-pharmacological interventions span a broader spectrum and can include anything from physical exercise to memory programs including those using assistive technology. However, there are multiple challenges when evaluating the effectiveness of interventions for cognition and cognitive-communication. First, there is no consensus regarding a definition of attention; currently, it is used as a general construct. Attention may also be divided into sub types (sustained, divided, focused, selective, vigilance, speed of information processing), however this is not always reflected in the literature. Second, researchers and clinicians may use different measures when reporting outcomes, making comparisons between interventions difficult. Third, a study may use the same outcome measures repeatedly, thereby confounding practice and treatment effects (e.g., performance on the Paced Auditory Serial Attention Task (PASAT) is known to improve with exposure). Finally, studies may not consider or account for the rate of spontaneous recovery following brain injury (i.e., natural recovery of function in the absence of treatment). For these reasons, assessing the efficacy of interventions for cognitive and cognitive-communication rehabilitation is more challenging compared to other modules due to the heterogeneous presentation within the population, plus variability in assessment of deficits. These challenges should be taken into consideration when interpreting concluding statements.

With respect to areas of cognitive-communication, and the role of the Speech-Language Pathologists (SLPs), there has been a significant expansion in the outcome research and clinical services over the past 15 years. It is apparent from this review that evidence-based research into therapeutic interventions is lagging in areas of cognitive-communication within the moderate to severe population. There is a limited number of high quality randomized controlled trials (RCTs) within the literature dedicated to cognitive-communication impairments in the moderate to severe ABI population and the therapies to assist with the improvement of these deficits. This is especially true for impairments related to linguistic organization, reading comprehension, written expression and information processing. In a review conducted by Perdices et al. (2006) on brain injury, it was found that the majority of studies (39%) were single subject designs, and only 21% were RCTs. Difficulties conducting RCTs with individuals who have sustained a moderate-severe ABI include the complexity of the disorder, the confounding effects of spontaneous recovery, the heterogeneity of this population, costs, specificity of treatment, the need for multifaceted integrated rehabilitation, and the informed consent procedure (Struchen, 2005; Wiseman-Hakes et al., 2010). Further, blinding participants to their treatment group, and team members who are responsible for providing the treatment is "*nearly impossible*" (Kennedy & Turkstra, 2006).

Bloom and Lahey (1978) define language as, *"knowledge of a code for representing ideas about the world through a conventional system of arbitrary signals for communication."* Language is comprised of some aspect of content or meaning that is coded or represented in a linguistic manner for the purpose of use in a particular context (Bloom & Lahey, 1978). Every aspect of language (content, form and use) includes cognitive processing. Impairment of any cognitive process may affect any or all components of language. It is the mutually dependent relationship between cognition and language that gives individuals the ability to generate, assimilate, retain, retrieve, organize, monitor, respond to and learn from the environment (Kennedy & Deruyter, 1991).

Traditionally, descriptions of communication disorders that exist within populations of individuals with ABI fall into four main groups: apraxia, aphasia, dysarthria and cognitive-communication. The term cognitive-communication disorder was adopted by the American Speech-Language-Hearing Association (American Speech-Language-Hearing Association, 1987) to distinguish the unique characteristics of communication post ABI from those of aphasia following stroke. The College of Audiologists and Speech-Language Pathologists of Ontario defines cognitive-communication disorders as: "…communication impairments resulting from underlying cognitive deficits due to neurological impairment. These are difficulties in communicative competence (listening, speaking, reading, writing, conversation, and social interaction) that result from underlying cognitive impairments (attention, memory, organization, information processing, reading, writing, problem solving and executive functions)" (p.4) (College of Audiologists and Speech Language Pathologists of Ontario, 2002). The study of language disorders following ABI has been challenging, conceivably more than any other area of communication disorders. SLPs are required to deal with issues of language use or pragmatics to a greater extent than for other acquired neurological communication disorders. In some instances, the language disorders found among individuals with ABI are more than just a reflection of underlying cognitive deficits. At other times, precise language processing deficits occur in conjunction with cognitively associated communication disorders (Kennedy & Deruyter, 1991).

Many individuals with an ABI, unlike individuals with developmental communication disorders, have a history of normal learning, reading, writing, language understanding and speech. Typically, they are younger than stroke survivors, and have greater concerns regarding transitions back to school and work along with everyday life activities. The mechanism of injury is often more diffuse and is related to a collection of cognitive-communication disorders as a result. Therefore, it is important to consider individuals with ABI as a distinct group (Turkstra, 1998). This is especially true in the moderate to severely impaired ABI group that is the focus of this evidence-based review.

In ABI, communication challenges are often observed along with otherwise intact speech, fluency, comprehension and grammar (Ylvisaker M & SF, 1994). The communication style of those with an ABI has

been described as “the language of confusion” (Halpern et al., 1973). In an older study, dysarthria was the most commonly diagnosed communication disorder (54%), followed by other cognitive communication deficits (16%), aphasia (4%) and apraxia of speech (4%) (Duffy, 2005).
Inappropriate/unconventional social behaviour or impaired executive function (e.g., self-awareness of strengths and weaknesses, goal setting, planning, self-initiating, self-inhibiting, self-monitoring, self-evaluating) are also common areas affected (American Speech-Language-Hearing Association, 1987).

This module addresses areas of cognition and cognitive-communication to the best of its ability in terms of organization and inclusion. It should be noted that these areas of functioning are closely intertwined not only because of dependence on the coordination of multiple areas of functioning to execute a specific task, but also because some areas of cognition and cognitive-communication remain poorly defined and understood.

6.1 Rehabilitation of Attention, Concentration, and Information Processing Speed

Although there is no specific agreement on the definition of attention, it is usually measured using externally directed tests, such as instructing participants to focus their attention on a sequence of stimuli or attenuating to a particular stimulus.

In general, TBI populations demonstrate significant deficits compared to control populations. Dymowski et al. (2015) showed that mild to severe TBI participants performed significantly worse on speed of information processing tasks compared to a healthy control group. Dockree et al. (2006) and Hasegawa and Hoshiyama (2009) found that TBI patients made significantly more errors than their non-TBI counterparts on dual task experiments for sustained attention. However, a case series by Foley et al. (2010) found that level of injury severity as measured by the Glasgow Coma Scale or PTA did not play a role in who performed poorly on the dual task assignment given to participants. They found that only 27% of TBI study participants performed below the cut-off for normal performance.

Two studies assessing the reaction times of individuals demonstrated that those with a TBI were found to have slower reaction times than individuals who had not sustained a TBI (Azouvi et al., 2004; Stuss et al., 1989). Results of the visual analogue scale also indicated that mental effort was higher for those with a TBI than for the controls. The results of this study confirmed what previous studies had found: those with a TBI have greater difficulty when dealing with two simultaneous tasks (Azouvi et al., 2004).

To better understand the mechanism by which cognitive interventions can improve attention, concentration, and information processing, there needs to be a consensus as to the definition of specific cognitive processes, including attention.

6.1.1 Non-Pharmacological Interventions

6.1.1.1 Drill and Practice

The following studies examined the influence of “drill & practice” exercises (either computerized and/or paper-and-pencil) on attentional functioning. Drill and practice training targets attention skills through repetitive training of specific tasks involving attention.

Table 6.1 The Effect of Drill and Practice on Attention Post ABI

Author Year Country Research Design PEDro Sample Size	Methods	Outcome
Novack et al. (1996) USA RCT PEDro=5 N=44	**Population:** Severe TBI; *Focused Stimulation Group (n=22)*: Mean Age=28.7yr; Mean Time Post Injury=5.9wk. *Unstructured Stimulation Group (n=22)*: Mean Age=26.4yr; Mean Time Post Injury=6.4wk **Intervention:** Participants were randomly placed into a focused or unstructured stimulation group. Patients in the focused group received hierarchical attentional learning training (30min, 5x/wk). Skills were not taught in a hierarchical or sequential fashion in the unstructured group. **Outcome Measure:** Digit Span and Mental Control subtests of Wechsler Memory Scale-Revised (WMS-R), computer-based simple and choice reaction time tests. *Secondary outcome measures*: Logical Memory I & II, Sentence Repetition, Judgment of Line Orientation, Trail Making A & B, Arithmetic subtest Wide Range Achievement Test-Revised, Visual imperceptions.	1. Analysis of primary outcome measures revealed no significant differences between the focused and unstructured stimulation groups, both at baseline and discharge. 2. There was a significant time effect with participants performing significantly better at the time of discharge than on admission (p<0.0001). 3. There were no significant differences between the groups with respect to any secondary outcome measures studied.
Lindelov et al. (2016) Denmark PCT $N_{Initial}$=78 N_{Final}=35	**Population:** ABI Group (n=17): Mean Age=56.1yr; Gender: Male=13, Female=4; Mean Time Post Injury=57d. Healthy Group (n=18): Mean Age=56.1yr; Gender: Male=8, Female=10. **Treatment:** ABI and healthy participants were randomized and analyzed separately. Experimental group participants received 20 sessions of N-back training (N-back), where participants press a key when presented stimulus is identical to the stimulus N back in the sequence. Control group participants received 20 sessions of visual search training (VS), where participants press a key if a target symbol is present in an NxN array of symbols. **Outcome Measure:** Raven's Advanced Progressive Matrices (RAPM), Wechsler Adult Intelligence Scale-IV (WAIS-IV), Working Memory Index (WMI Index, digit span, arithmetic, letter-number sequencing), Operation Span Test (OSPAN), WAIS-IV Processing Speed Index (PSI index, search, coding), Stroop Test.	1. Both ABI and healthy groups showed significant improvement post-intervention on the assigned training tasks (Bayes factor >> 1000). The standardized mean difference was 0.45 for ABI N-back, 6.11 for healthy N-back, 1.06 for ABI VS, and 3.34 for Healthy VS. The healthy group showed greater improvement than the ABI group (Bayes factor >> 1000). 2. No significant differences in improvements between N-back and VS treatments (time x treatment interaction) were found in ABI or healthy groups for WMI-digit span, WMI-arithmetic, WMI-letter-number sequencing, WMI index, PSI-search, PSI-coding, PSI index, RAPM, OSPAN, or Stroop. 3. No significant differences in improvement between healthy and ABI groups (group x time x test interaction) were found for WMI-digit span, WMI-arithmetic, WMI-letter-number sequencing, WMI index, PSI-search, PSI-coding, PSI index, RAPM, OSPAN, or Stroop.

PEDro = Physiotherapy Evidence Database rating scale score (Moseley et al., 2002a).

Discussion

The two studies desmontrated no significant differences between groups for attentional, functional, and/or cognitive skills assessed (Lindelov et al., 2016; Novack et al., 1996). Novack et al. (1996) compared focused hierarchical attentional learning with an unstructured non-sequential, non-hierarchical intervention, while Lindelov et al. (2016) compared N-back training with visual search training. Novack et al. (1996) found that there were no significant differences between groups at either time points; however, both groups significantly improved over time. Although the study by Lindelov et al. (2016) also found no significant treatment effects over time, in contrast to the previous study, no spontaneous recovery effects were found either. Overall, there is weak evidence in support of training programs as an effective rehabilitation intervention for attention.

Conclusion

There is level 2 evidence that drill, and practice training may not be effective for the remediation of attention compared to spontaneous recovery, regardless of the level of structure in the program for those with an ABI.

Drill and practice training may not be effective for the remediation of attention following an ABI.

6.1.1.2 Dual-Task Training

The following studies examined the effect of "dual-task" training on speed of processing. Dual-task training involves dividing attention between two stimuli in order to complete two tasks concurrently and successfully, such as walking while speaking.

Table 6.2 The Effect of Dual-Task Training on Speed of Processing Post ABI

Author Year Country Research Design PEDro Sample Size	Methods	Outcome
Couillet et al. (2010) France RCT PEDro=5 N=12	**Population:** severe TBI; Gender: Male=9, Female=3. *Group 1 (n=5)*: Mean Age=23.8yr; Mean GCS=4.8; Mean Time Post Injury=6.3mo. *Group 2 (n=7)*: Mean Age=26.7yr; Mean GCS=4.8; Mean Time Post Injury=16.1mo. **Intervention:** Randomized AB versus BA design, where "A" represents the control phase and "B" represents the treatment (dual-task training) phase. In the dual-task phase, patients were trained to conduct two concurrent tasks simultaneously. Group 1 started with the control phase (AB) and Group 2 (BA) with the treatment phase. Each phase lasted 6 wk (4, 1 hr sessions/wk). **Outcome Measure:** Test Battery for Attentional Performance (TAP: divided attention and flexibility subtests), Go-no go and Digit Span, Trail Making Test, Stroop Test, Brown-Peterson Paradigm, Rating Scale of Attentional Behaviour.	1. Following training, there was a significant improvement in the 2 tasks that targeted divided attention (TAP-divided attention, Go-no go and Digit Span: p<0.0001 for both). 2. The two groups differed significantly at 6 wk with those in the BA design doing better on TAP reaction times (p<0.01), the digit span dual-task (p<0.001), and the Rating Scale of Attentional Behaviour (p<0.01). 3. There were significant differences between groups at 6 wks on the Stroop test (p<0.001) and the flexibility subtest of the TAP (p<0.001), but not the Trail Making Test or the Brown-Peterson task. 4. Experimental training had no significant effects on non-target measures.
Stablum et al. (2000) Italy Case-Control N=38	**Population:** Condition: Chronic Head Injury (CHI)=10 [mean age:25.6 yr, time since injury: 27.8 months]. Anterior Communicating Artery Aneurysm	*CHI study:* 1. Significant difference between patients and controls on number of preservative errors

Author Year Country Research Design PEDro Sample Size	Methods	Outcome
	(ACoA)=9 [mean age: 43.22 yr, time since injury=3.66 months]. Controls=19 (CHI study n=10, ACoA study n=9; Age Range: 14-68yr). **Intervention:** *CHI study:* Neuropsychological assessments (i.e., Wisconsin Card Sorting Task (WCST), Paced Auditory Serial Addition Task (PASAT)) were conducted. As well as a Dual-Task Paradigm: Participant had to indicate the position (right or left) of the stimuli and saying aloud if stimuli were congruent. Participants were evaluated at baseline, retest after treatment, and at 3 months follow-up. *ACoA study:* Neurological Assessments and Dual-task paradigm were conducted similar to the CHI study, but participants also performed a Continuous Performance Task (CPT) measuring inhibition responses in executive functioning. Participants were evaluated at baseline, retest after treatment, and at 3 months and 12 months follow-up. **Outcome Measure:** WCST, PASAT, CPT, dual-task cost.	($p<0.017$) and categories ($p<0.020$) achieved in WCST, and PASAT mean time ($p=0.031$). 2. Reaction time was slower for CHI patients than controls in dual-task ($p<0.005$); dual task cost significantly greater for CHI patients than controls ($p<0.028$). 3. At retest and at 3-months follow-up reaction time was slower for CHI patients than controls ($p<0.0001$); but patients demonstrated a greater reduction in dual-task cost after treatment (54 vs 22 ms). *ACoA Study:* 4. ACoA patients had slower reaction times than controls on CPT ($p<0.001$). 5. Reaction time for closed head injury ($p<0.0001$) and aneurysm ($p<0.007$) group significantly slower than control. 6. Inhibiting a habitual response took ACoA patients significantly longer than controls on the CPT ($p<0.011$). 7. The dual-task cost was greater for the ACoA group compared to the control group ($p<0.0001$). 8. The dual-task cost was significantly greater at assessment than at retest, 3, and 12-month followup ($p<0.0001$); after treatment ACoA patients could co-ordinate two responses as efficiently as controls at 6-month re-assessment.

PEDro = Physiotherapy Evidence Database rating scale score (Moseley et al., 2002a).

Discussion

One RCT with a TBI population showed that attention and information processing outcomes could be improved within the dual task paradigm (Couillet et al., 2010). Couillet et al. (2010) found that dual-task training significantly improved attentional behaviour and reaction time compared to a non-specific cognitive program. Stablum et al. (2000) found that initially individuals with a closed head injury (CHI) performed poorly on dual-task measures; however, with additional training their completion time of dual-task measures significantly increased compared to the control group.

Conclusion

There is level 2 evidence that dual task training may be effective in improving attention task performance in ABI populations compared to non-specific training.

Dual-task training has been shown to improve measures of attention to the extent that the ABI population does not significantly differ from healthy controls, however it is undetermined if the strength of these effects compared to non-dual-task training are greater.

6.1.1.3 Technological Interventions

A surge in technology has allowed for the development of more computer-based intervention solutions designed to improve attention, concentration, and information processing. Current treatment modalities include computer cognitive training programs and virtual reality sessions. Virtual reality is discussed in further detail in 6.2.1.1.3 where its effects on learning and memory are presented.

Table 6.3 The Effect of Computer-Based Interventions on Reaction Time Post ABI

Author Year Country Research Design PEDro Sample Size	Methods	Results
Dirette et al. (1999) USA RCT PEDro=4 N=30	**Population:** TBI: Mean age=38yr; Gender: male-22, female-8; Time since injury range=2-12 months. **Intervention:** Randomly assigned to remedial (without instruction, n=15) and compensatory strategy (verbalization, chunking and pacing) intervention (n=15) groups receiving a 45-minute session once a week for 4 weeks. **Outcome Measure:** Pre and Post-test on the Paced Auditory Serial Addition Task (PASAT).	1. Pre/post and weekly tasks significantly improved in both groups (p<0.01). 2. No significant improvement due to intervention (p>0.05).
Grealy et al. (1999) Scotland RCT PEDro=1 N=13	**Population:** TBI patients: Age Range: 19-64; Gender: male=8, female=5. **Intervention:** Crossover design: patients were allocated to 4-week interventions of receiving a single bout of Virtual reality (VR) exercise or a no-exercise control condition. **Outcome Measure:** Tests measuring attention, information processing, learning, memory, and reaction and movement times.	1. Intervention group (n=13) performed significantly better than control group (n=320) on digit symbol (p<0.01), verbal (p>0.01) and visual (p<0.05) learning tasks. 2. Reaction (p<0.01) and movement (p<0.05) times improved significantly after a single VR session.
Ruff et al. (1994) USA RCT PEDro=3 N=15	**Population:** Severe head injury; Mean Age=26.9yr; Time Post Injury≥6mo. **Intervention:** Participants were randomized to one of two treatment conditions: attention training followed by memory training (Group A; n=7) or vice versa (Group B; n=8). Training was provided from THINKable, a computer-based multi-media program. Training was terminated after either 20 hr (2hr/d) were completed, or 90% scores were achieved on the most advanced program. Patients were assessed before, during and after training. **Outcome Measure:** 2 + 7 Selective Attention Test, WAIS-R Digit Symbol, Continuous Performance Test (CPT); Rey Auditory Verbal Learning Test,	1. Computer-based attention training resulted in significant improvements for attention (p=0.003). 2. Significant improvement in Memory II (p=0.021) but not Memory I or III. Gains were significant for Rey Verbal (p=0.004) and Corsi Block Learning (p=0.03) total correct as well. 3. Significant improvements in digital symbol scores (p<0.001) were noted as well, but no significant changes were found with CPT or 2+7 test scores.

	Corsi Block Learning Test.	
Gray et al. (1992) UK PEDro=5 N=31	**Population:** Close Head Injury=17; Others=14. *Experimental Group (n=17)*: Mean Age=26.18yr; Gender: Male=12, Female=5; Mean Time Post Injury=79wk. *Control Group (n=14)*: Mean Age=34.14yr; Gender: Male=10, Female=4; Mean Time Post Injury=84wk. **Treatment:** Participants in the experimental group received micro-computerized attentional training (1-1.5hr sessions for 3-9wk). The training covered reaction time training, rapid number comparison, digit symbol transfer, and divided attention tasks. The control group received recreational computing for a similar time period. **Outcome Measure:** Digit Span, Backward Digit Span, Paced Auditory Serial Addition task (PASAT), Information Processing Rate (IRP), Longest string, Wisconsin Card Sorting Test, Wechsler Adult Intelligence Scale-Revised (WAIS-R) Arithmetic.	1. At post-test assessment, the experimental group showed significant improvement on the WAIS-R picture completing (p=0.031) and the PASAT information processing rate (p=0.023). 2. At the 6 mo follow-up, differences between the groups indicated significant improvement on the Backward Digit Span (p=0.007), the WAIS-R Arithmetic (p=0.014), information processing rate and the PASAT (p=0.011), longest string (p=0.009), IPR (p=0.019). 3. For the experimental group, improvements from the intervention were found for IPR (p=0.004). 4. In general, course improvement was seen in the experimental group during the intervention phase and was continued into follow-up.
Dahdah et al. (2017) USA Pre-Post $N_{Initial}$=21 N_{Final}=15	**Population:** CVA=6, TBI=5, Tumor=2, Anoxia brain injury=2; Mean Age=40.3yr; Gender: Male=12, Female=3. **Intervention:** Participants received the virtual reality (VR) intervention sessions (apartment and classroom) twice per week for a 4wk period. Sessions 1 and 8 included all types of distractors, sessions 2 and 3 included no distracting stimuli, sessions 4 and 5 included only auditory distracting stimuli, and sessions 6 and 7 included only visual distracting stimuli. **Outcome Measure:** Woodcock-Johnson, 3rd edition (WJ-III pair cancellation subtest), Delis-Kaplan Executive Function System (D-KEFS Color-Word Interference subtest), Automated Neuropsychological Assessment Metrics (ANAM Go/No-Go and unimodal Stroop subtests), VR Stroop task (apartment and classroom).	1. No statistically significant performance differences were found from baseline to conclusion of the study for the VR apartment Stroop or D-KEFS Stroop test. 2. For the VR classroom, participants' shortest response time on the word-reading condition was significantly reduced by session 8 (p=0.0383). All other VR classroom Stroop variables did not show significant differences. 3. No significant differences from session 1 to session 8 were found for all pair cancellation subtest scores. 4. From session 1 to 8, the ANAM Stroop word-reading percentage of items with a correct response (p=0.0293), ANAM Stroop word-reading number of correct responses per minute (p=0.0321), and ANAM Go/No-Go number of impulsive/bad responses (p=0.0408) significantly increased. All other ANAM variables did not show significant differences.
O'Neil-Pirozzi and Hsu (2016) PCT $N_{Initial}$=14 N_{Final}=12	**Population:** TBI=4, CVA=2, Brain tumour=1; Severity: moderate/severe. *Experimental Group (n=7)*: Mean Age=51.3yr; Gender: Male=5, Female=2; Mean Time Post Injury=20.9yr; Etiology: TBI=5, CVA=2. *Control Group (n=7):* Mean Age=46.9yr; Gender: Male=7; Mean Time Post Injury=25.0yr. **Intervention:** Experimental group participants received BrainHQ, a commercially available online computerized cognitive exercise program (Attention, Brain Speed, Memory, People Skills, Intelligence, and Navigation) for 5 mo, 5d/wk. Control group participants did not have a private computer and received no intervention. **Outcome Measure:** Number/percentage of sessions completed, Number/percentage of	1. Of the five experimental group participants that completed the study, they completed an average 87% of sessions, initiated an average 25% of sessions, and independently completed an average 7% of sessions. Two participants needed minimum external cues, two participants needed moderate external cues, and one participant needed maximum external cues. 2. Comparing 3mo prior to intervention with 1wk prior to intervention, there were no significant differences within either group for WCST, HVLT-R, COWAT, TMT A or B, or SWLS. 3. There were no significant differences between groups at 1wk prior to intervention

	sessions initiated by participants, Number/percentage of sessions completed independently by participants, Mean amount of external cures provided for session completion, Wisconsin Card Sorting Test (WCST), Hopkins Verbal Learning Test-Revised (HVLT-R immediate, delayed), Controlled Oral Word Association Test-FAS (COWAT), Trail Making Test (TMT A and B accuracy and speed), Satisfaction with Life Scale (SWLS), Semi-structured interview questions.	(baseline) for WCST, HVLT-R, COWAT, TMT A or B, or SWLS. 4. Compared to baseline, experimental group showed significant improvement post-intervention for HVLT-immediate (p=0.0255) and SWLS (p=0.0075). There were no significant improvements for WCST, HVLT-delayed, or TMT A or B. 5. Compared to baseline, control group did not show significant differences post-intervention for WCST, HVLT, TMT A or B, or SWL. 6. Compared to control group, experimental group showed significantly higher post-intervention improvements on HVLT-immediate (p=0.0068) and COWAT (p=0.0310). No significant differences between groups were found for changes in WCST, HVLT-delayed, TMT A or B, or SWL. 7. Of the experimental group participants who completed the study, 60% reported improved everyday thinking abilities, 60% reported improved memory, and 20% reported improved attention, organization, and/or problem-solving skills, but 60% reported they would not continue with exercise program post-study completion.
Li et al. (2015) USA Pre-Post $N_{Initial}$=13 N_{Final}=12	**Population:** Stroke=5, TBI=5, Brain tumor=2; Mean Age=61yr; Gender: Male=10, Female=2. **Intervention:** Participants received the computer-based cognitive retraining program, Parrot Software. The following eight modules were each completed in separate 1h sessions: Visual Instructions, Attention Perception and Discrimination, Concentration, and Visual Attention Training, Remembering Written Directions, Remembering Visual Patterns, Remembering Written Letters, and Remembering Written Numbers. **Outcome Measure:** Montreal Cognitive Assessment (MoCA overall, attention, memory), Medication-box sorting task.	1. Compared to baseline, there was a significant mean increase in overall MoCA of 3.25 (p=0.03) post-intervention. However, the attention and memory subscales did not show significant differences. 2. There were no significant differences before and after intervention for the medication-box sorting task. 3. Participants with previous computer-based cognitive retraining experience had significantly more MoCA improvement than those without (p<0.01). 4. Age, education level, or type of ABI diagnosis did not have any significant effects on MoCA or medication-box scores.
Gerber et al. (2014) USA Pre-Post N=19	**Population:** TBI; Mean Age=50.4yr; Gender: Male=11, Female=8; Mean Time Post Injury=10yr; GCS=4-14; Severity: Severe=9, Moderate=1, Mild=7. **Intervention:** Participants completed a series of virtual reality tasks in a standardized order utilizing a hepatic stylus; 1) Participants were asked to clear a workbench and mount tools on an upright pegboard (TOOL), then 2) spell as many 3-letter words as possible from a set of letter tiles (SPELL), then 3) prepare a virtual peanut butter and jelly sandwich (SAND), and finally 4) hammer in two nails and tighten two screws through tool use (TUSE). TOOL, SAND and TUSE tasks had a time limit of 5 minutes while SPELL task had a time limit of 2 minutes.	1. All the participants reported a high level of engagement during the interactions. 2. Thirty percent of participants reported a high level of frustration but were able to complete the tasks with short breaks. 3. From baseline to final, TOOL mean time decreased by 60s, TUSE mean time decreased by 68s, SAND mean time decreased by 72s and SPELL means increased by 2.7 words. 4. PPT correlated with TOOL (p=0.016) and TUSE (p=0.014) time during the final trial. 5. SPELL correlated with the BPS (p=0.08) during the baseline and NSI (p=0.05) during the final trial.

	Participants had 3 chances to perform each task (Baseline, 2nd, Final). **Outcome Measure:** Self-reported measures (engagement and frustration), Boredom Propensity Scale (BPS), Purdue Pegboard Test (PPT), and Neurobehavioural Symptom Inventory (NSI).	
Dvorkin et al. (2013) USA Pre-Post N=21	**Population:** TBI; Mean Age=37.8yr; Gender: Male=17, Female=4; Mean Time Post Injury=10.3wk. **Intervention:** Participants completed a virtual reality task and were instructed to hold the handle of a robot, moving the handle towards targets that appeared in the virtual environment. Patients reached to as many targets as they could within 4 minutes (1 block). Participants completed 6 blocks per day for 2 consecutive days. On each day, each pair of blocks included one haptic condition that affected the robotic handle and was either; 1) no haptic feedback (no force condition), 2) a break-through force, similar to popping a balloon (break-through condition) or 3) a gentle pulse of force (nudge condition). **Outcome Measure:** Tolerance, attention (pauses, pause duration), number of targets reached, and Agitated Behaviour Scale (ABS).	1. The interactive virtual environment was well tolerated by 18 of the 21 patients, 3 participants could not complete the 6 blocks in each visit due to fatigue or frustration. 2. In 15 participants ABS was reduced on the second visit. 3. Attention loss was reported before and during arm movements, however on the second visit patients exhibited significantly less pauses (p<0.0001) and shorter pause duration (p=0.007). 4. Patients were able to reach more targets on the second visit compared to the first visit (p<0.0001). 5. During the first visit, participants reached significantly less targets in the break-through and no force conditions compared to the nudge condition (p<0.02); the break-through and no force conditions were not significantly different. 6. During the second visit, participants reached significantly more targets in the nudge and no force conditions compared to the break-through condition (p<0.002); the nudge and no force conditions were not significantly different. 7. Break-through trials were significantly longer then the no force and nudge conditions on both the first and second day (p<0.0001). 8. Participants acquired more targets during the second visit compared to the first (p=0.0003) and acquired more targets with each block (p<0.0001).
Li et al. (2013) USA Pre-Post N=11	**Population:** ABI; Mean Age=49.45yr; Mean Time Post Injury=21.27yr. **Intervention:** All participants completed eight 60-min sessions using the attention and memory sub programs of the computer-based cognitive retraining Parrot Software. The participants focused on one of the eight subprograms during each session with each subprogram containing 10 lessons with increasing difficulty. Assessments were conducted before and after intervention. **Outcome Measure:** The cognitive assessment (attention & memory).	1. There was a significant improvement in attention cognitive assessment scores from pre to post intervention (mean change=2.091; p<0.005). 2. There was a significant improvement in memory cognitive assessment score from pre to post intervention (mean change=1.73; p<0.05).
Zickefoose et al. (2013) USA Pre-Post N=4	**Population:** TBI; Mean Age=42.75yr; Gender: Male=4, Female=0; Mean Time Post Injury=17.5yr; Severity: Severe=4, Moderate=0. **Intervention:** Participants engaged in computer-based brain games over the course of two 1-month treatment phases. Participants received	1. All four participants demonstrated significant progress in reaching new levels of difficulty on all tasks over the course of both treatments (p<0.01). 2. NAB analysis showed that one participant demonstrated significant improvement on

	Attention Process Training-3 (APT-3) or Lumosity™ in phase 1, and then received the alternate treatment in phase 2. Both phases consisted of twenty 30-minute sessions. Outcomes were assessed at baseline and after each phase. **Outcome Measures:** Test of Everyday Attention (TEA); Neurological Assessment Battery (NAB)–Numbers and Letters Test Parts B, C, and D; Perceptual rating scale (PRS).	one sub-test, while two participants demonstrated non-significant improvement on one or more sub-tests. Improvements occurred during phase 1, regardless of treatment. 3. TEA analysis showed that one participant demonstrated improvement on several sub-tests during both treatments, while the scores of the other three participants were inconsistent for either treatment. 4. On the PRS, two participants showed strong enjoyment and willingness to continue APT-3, while the other two participants showed an equally strong rejection of ATP-3. 5. On the PRS, all four participants showed strong enjoyment of Lumosity™, while only two participants showed a strong willingness to continue.
Chen et al. (1997) USA Case-Control N=40	**Population:** Age=18+years; Gender: male=27, female=13; Condition: TBI. **Intervention:** Divided retrospectively into computer-assisted rehabilitation (CACR) and tradition therapy groups **Outcome Measure:** Neurophysiological test scores (WAIS-R; WMS).	1. Both groups made significant post-treatment gains on the neurophysiological test scores ($p<0.05$), with the CACR group making significant gains on 15 measures ($p<0.05$) and the comparison group making significant gains on seven measures ($p<0.005$). 2. However, no significant difference was found between groups on their post-treatment gains.
Malec et al. (1984) United States RCT Crossover PEDro=8 N=10	**Population:** Mean age=30yr; Gender: Male=8, Female=2; Mean time post injury=80dys. **Intervention:** Individuals played two types of first-person shooter video games, one with no interfering targets and one with them present. Individuals were randomly assigned to treatment order. Video game conditions were 1 week-long and included twice daily sessions of video game play. **Outcomes:** Stroop Test, Letter Cancellation task, Symbol Cancellation task, reaction time (RT).	1. No significant differences were found between conditions at any time points.

PEDro = Physiotherapy Evidence Database rating scale score (Moseley et al., 2002a).

Discussion

An RCT by Dirette et al. (1999) found no significant differences in improvements between participants taught specific compensatory strategies and those that simply completed the computer tasks without instruction of compensatory strategies. However, both groups significantly improved over time, with those that used the compensatory strategies (whether taught or spontaneously acquired) performing better than those that did not (Dirette et al., 1999). Similarly, Chen et al. (1997) studied the effect of computer assisted cognitive rehabilitation versus traditional therapy methods. While measures of attention significantly improved in both groups after treatment, no significant differences were observed between groups (Chen et al., 1997). Other studies with brand name computer-assisted cognitive rehabilitation have also shown limited effects. A small pre-post study examining the program Luminosity™ showed improvements in attention for a minority of participants; however, this improvement did not significantly differ from those who received Attention Process Training-III (Zickefoose et al., 2013). Parrot software showed mixed results with a pilot study reporting significant improvement in attention post-intervention (Li et al., 2013), but a subsequent study reported no significant changes on measures related to attention (Li et al., 2015). BrainHQ did not significantly improve attention outcomes over time or compared to no intervention (O'Neil-Pirozzi & Hsu, 2016). The lack of evidence supporting the efficacy of computer-based cognitive rehabilitation may be due to different programs and strategies used to train participants.

Repetition of tasks in virtual reality improved performance, both in terms of speed and accuracy (Dvorkin et al., 2013; Gerber et al., 2014). Gentle nudges corrected behaviour better than break-through or no feedback (Dvorkin et al., 2013). However, repetition of the Stroop test in different virtual reality environments showed limited improvement in performance on those specific tests (Dahdah et al., 2017). A virtual reality exercise program demonstrated significant benefits in reaction times but not attention after intervention; more high quality research is needed to confirm the efficacy of virtual reality exercise (Grealy et al., 1999).

Conclusions

There is level 2 evidence that neither general nor name brand computer-based rehabilitation intervention may improve attention outcomes compared to usual care in ABI populations.

There is level 4 evidence that attention performance can be improved in ABI populations through repetition of tasks, either through computer-based or virtual reality environments.

Computer-based interventions are no more effective than no intervention in improving measures of attention and concentration post ABI.

Repetitive virtual reality tasks which include repetition are effective in improving attention and concentration in ABI populations.

6.1.1.4 Attention Training Programs

With regard to cognitive rehabilitation, therapy is typically patient-directed and driven by both long- and short-term goals (Carswell et al., 2004). The ability to self-direct towards goals is emphasized as a component of brain injury community reintegration programs and is integral in the completion of instrumental activities of daily living. The execution of these goals relies on an individual having the ability to focus attention on a given task.

Cicerone et al. (2005) recommended strategy training for persons with TBI for improving deficits of attention. It should be noted, however, that there was insufficient evidence to distinguish the effectiveness of specific attention training during acute stage rehabilitation from improvements made from spontaneous recovery or from more general cognitive interventions (Cicerone et al., 2005).

Table 6.4 The Effect of Attention Training Programs on Attention and Concentration Post ABI

Author Year Country Research Design PEDro Sample Size	Methods	Results
Gocheva et al. (2018) Switzerland RCT Crossover PEDro=7 N=19	**Population:** Non-traumatic etiology (N=13), traumatic etiology (N=9). **Intervention:** All participants received both conditions in randomized order, each condition consisted of 12 sessions. The experimental condition consisted of speech, occupational or physical therapy sessions accompanied by a therapeutic animal, while the control condition consisted of the same rehabilitation interventions and did not include a therapeutic animal. All conditions were completed within 6 weeks. **Outcome Measures:** Attention span, alertness, instances of distraction, and concentration (all outcomes were measured through behavioral analysis).	1. Attention span did not differ significantly between experimental and control sessions. 2. When in the animal therapy sessions individuals displayed significantly more instances of distraction compared to control sessions (p=0.001). Physiotherapy sessions were significantly more effected by distractions when animals were present (p=0.016). Further analysis demonstrated that those with higher initial FIM scores had significantly decreased instances of distraction in animal therapy sessions (p=0.003). 3. During animal therapy sessions self-assessed alertness was significantly higher (p<0.001). There was also a significant main effect of therapy, with higher alertness in speech therapy sessions overall (p=0.012). Alertness was also significantly higher in the animal therapy session when individuals had higher initial FIM scores, than those that did not in animal sessions (p<0.001). 4. Individuals had significantly higher rates of self-reported concentration during animal therapy sessions (p=0.014). Concentration was also seen to be significantly higher in speech therapy sessions regardless of animal presence (p=0.027), with therapy type overall having a significant effect (p<0.001), but no significant interaction effect. Individuals with higher initial FIM scores demonstrated higher concentration scores in sessions when animals were present compared to those who had lower initial FIM scores (p<0.001).
Dundon et al. (2015) Ireland RCT PEDro=3 N=26	**Population:** TBI; Mean Age=38.96yr; Gender: Male=19, Female=7. **Intervention:** Participants were assessed during a dichotic listening task (DLT) presented at 6 levels of distraction difficulty, and randomly received either adaptive training (AT, n=9), non-adaptive training (NAT, n=8), or no training (NT, n=9) between sessions (Study 2). Outcomes were assessed before and after training. **Outcome Measures:** DLT performance; Test of Everyday Attention (TEA).	1. For the DLT, there was a significant main effect of group (F=3.99, p=0.035), such that the AT group showed poorer performance than the NAT group (p=0.019) and the NT group (p=0.031). 2. For the DLT, there was a significant interaction between group and time (F=4.38, p=0.026), such that improved performance was seen in the AT (p=0.036) and NAT (p=0.0025) groups over time, but not in the NT group (p=0.34). 3. On the TEA, there was a significant main effect of group (F=2.45, p=0.13), such that the NT group showed better performance than the AT group (p<0.001) and the NAT group (p=0.036).

		4. On the TEA, there was a significant main effect of time (p=0.022), such that performance improved in all groups.
Cantor et al. (2014) USA RCT PEDro=7 N=98	**Population:** TBI; Mean Age=45.3yr; Gender: Male=37, Female=61; Mean Time Post Injury=12.6yr; Severity: Mild=49, Moderate=19, Severe=30. **Intervention:** Participants were randomly assigned to either immediate start (IS; n=49) or waitlist control (WL; n=49) groups. Participants received group sessions of emotional regulation (2 sessions, 45min) and an individual problem-solving session of attention training (1 session, 60min) per day (3 days/wk for 12 weeks). Group sizes were generally 4-6 participants. **Outcome Measures:** Attention Rating and Monitoring Scale (ARMS), Behavioural Assessment of the Dysexecutive Syndrome, Difficulties in Emotion Regulation Scale (DERS), Executive Function Composite from Factor Analysis (EF index), Problem Solving Inventory (PSI), and Frontal System Behavioural Scale (FrSBe).	1. There was a significant treatment effect for the EF index favoring the IS group (p=0.008). 2. There was no significant difference between groups in the DERS of ARMS. 3. Secondary analysis revealed a significant treatment effects for the FrSBe scale (p=0.049) and the PSI (p=0.016). 4. There were no other significant treatment effects. Variance of depression, age, severity and time since injury did not change treatment effects.
McHugh and Wood (2013) Ireland RCT PEDro=5 N=24	**Population:** TBI. *Mindfulness Group (N=12)*: Mean Age=28.45yr; Mean Time Post Injury=785.5d; Mean GCS=8.5. *Control group (N=12)*: Mean Age=30.5yr; Mean Time Post Injury=664.7d; Mean GCS=7.42. **Intervention:** Patients were randomly assigned to the control group or mindfulness group (focused attention). The mindfulness group received instructions (mindfulness induction) prior to completing experimental tasks. Participants then completed a memory load task (remembering the location of symbols) and an over-selectivity task and test. **Outcome Measures:** Minimal Attention Awareness Scale (MAAS), Trail making test A and B (test of visual attention and task switching) and the Wechsler Test of Adult Intelligence.	1. There was a significant decrease in stimulus over-selectivity after the mindfulness training compared to the control group (p<0.05, t (22) =1.74).
Chen et al. (2011) USA RCT PEDro=5 N=12	**Population:** TBI=9, Other=3: Mean Age=48yr; Gender: Male=5, Female=7; Time Post-Injury Range=6mo-6yr. **Intervention:** Participants were randomized to receive either the goals training intervention (n=7) or education intervention (n=5) for 5 wk, after which they switched to the other condition for another 5 wk. The goals training was spread over 5 wk and involved: group, individual and home-based training. The education program was a 5 wk didactic educational instruction regarding brain injury. **Outcome Measures:** Letter number sequencing, Wechsler Adult Intelligence Scale-III, Auditory consonant trigrams, Digit Vigilance Test, Design and Verbal Fluency Switching, Trails B, Stroop Inhibition, Hopkins Verbal Learning Test, Brief	1. On the domain of attention and executive functions, all participants in the goal training intervention showed an increase from pre to post goals training; while only 7/12 in the education intervention showed an increase from pre to post education (p<0.0001). 2. For learning and memory performance scores increased an average of 0.70 units after participation in goals training than after participation in education intervention (p=0.02). 11/12 participants improved in the goals training group while 4/12 improved in the education group (p=0.009). 3. Tests of motor speed of processing showed no significant differences between the two interventions with a non-significant trend

	Visual Memory Test Revised, Trails A test, Visual Attention Task.	for greater improvements in goal-training compared to education (p=0.07).
Novakovic-Agopian et al. (2011) USA RCT Crossover PEDro=5 N=16	**Population:** TBI=11, Stroke=3, Other=2: Mean Age=50.4yr; Gender: Male=7, Female=9; Time Post Injury Range=1-23yr. **Intervention:** Participants were randomized to 5 wk interventions consisting of a goals training program (n=8) or an educational instruction group (n=8). Goal training focused on mindfulness-based attentional regulation and goal management strategies for participant-defined goals. Educational training was didactic instructional sessions about brain injury. At the end of 5wk, participants were switched to the other intervention. All participants were assessed at baseline, Week 5 and again at Week 10. **Outcome Measures:** Auditory Consonant Trigrams, Letter Number Sequencing (working memory); Digit Vigilance Test (sustained attention); Stroop Inhibition Delis-Kaplan Executive Function System (Inhibition); Trails B, Design Fluency-switching (mental flexibility), Hopkins Verbal Learning Test-Revised, Brief Visual Memory Test-Revised.	1. At the end of wk 5 participants in the goals-edu group showed significant improvement on measures of attention and executive function from baseline (p<0.0001), while the edu-goals group showed no change or minimal change (p>0.05). 2. The goals-edu group had significantly greater improvements than the edu-goals group on the following at wk 5: working memory (*Mean* 1.12 vs -0.12, p<0.0001); mental flexibility (*Mean* 0.64 vs 0.04, p=0.009); inhibition (*Mean* 0.62 vs 0.04, p=0.005); sustained attention (*Mean* 0.96 vs 0.27, p=0.01); learning (*Mean*=0.51 vs 0.08, p=0.02); and delayed recall (*Mean* 0.39 vs -0.27, p=0.01). 3. At wk 10, the edu-goals group significantly improved compared to wk 5 on: attention and executive function (0.79 vs 0.03, p<0.0001); working memory (1.31 vs -0.12, p<0.0008); mental flexibility (0.66 vs 0.04, p<0.0008); inhibition (0.50 vs 0.04, p=0.01); sustained attention (0.44 vs 0.27, p=0.01); memory (0.609 vs -0.10, p=0.02); learning (0.66 vs 0.08, p=0.05); and delayed recall (0.55 vs -0.27, p=0.02). 4. Those in the goals-edu group who had completed the training session were able to maintain their gains and there were significant improvements in attention and executive function (p<0.04) and working memory (p<0.02).
McMillan et al. (2002) UK RCT PEDro=5 N=130	**Population:** TBI*; Attentional Control Training (ACT; n=44):* Mean Age=34.6yr; Gender: Male=35, Female=9; Median GCS=9. *Physical Exercise (PE) Group (n=38)*: Mean Age=31.4yr; Gender: Male=30, Female=8; Median GCS=10. *Control Group (n=48)*: Mean Age=36.2yr; Gender: Male=36, Female=12; Median GCS=9 **Intervention:** Patients were assigned to 1 of 3 groups. The ACT group received supervised practice (5, 45min session over 4wk) and were given an ACT audiotape to practice daily with. The PE group had the same amount of therapist contact, but the audiotape was based on physical training. The control group had no therapist contact. Assessments were done pre- and post-training, and 6 and 12mo. **Outcome Measures:** Test of Everyday Attention, Adult Memory and Information Processing Battery, Paced Auditory Serial Addition Test, Trail Making Test, Sunderland Memory Questionnaire, Cognitive Failures Questionnaire.	1. Results showed no significant differences in outcome measures among the 3 training groups at any of the assessment points. 2. The exception to the above finding was the results of the Cognitive Failure Questionnaire where patients in both treatment groups (ACT and PE) had significantly greater reduction in self-reported cognitive failures compared to the control group at 12 mo follow-up (p<0.05).
Amos (2002) Australia	**Population:** TBI=16, CVA=6, Other=2, Healthy Controls=8. *Experimental Group (n=24)*: Mean Age=35.71yr; Gender: Male=17, Female=7; Mean	1. There were no significant differences in total errors between groups (p=0.138), but groups differed significantly in total number

RCT PEDro=4 N=32	Time Post Injury=5.96yr. *Control Group (n=8)*: Mean Age=31.25yr; Gender: Male=2, Female=6. **Intervention:** Patients with ABI were randomized into three treatment groups: unaided (n=8), external inhibition (n=8), and increased stimulus salience (n=8). All treatment groups were compared to the non-ABI controls (n=8). **Outcome Measures:** Wisconsin Card Sorting Test (WCST).	of trials (p=0.025), perseveration (p=0.033) and categories achieved (p=0.001). 2. The unaided ABI group compared to the aided ABI group (inhibition and salience) had significantly more trials (p<0.001), preservative errors (p<0.006) and lower categories score (p<0.001). 3. Comparisons between the inhibition and salience aid group revealed significance difference only for perseverative errors (p<0.045); the external inhibition group displayed much less.
Levine et al. (2000) Canada UK RCT PEDro=4 N=30	**Population:** TBI: *Goal Management Training (GMT) Group* (n=15): Mean Age=29.0yr; Gender: Male=5, Female=10; Mean GCS=10.7; Mean Time Post Injury=3.7yr. *Motor Skill Training (MST) Group* (n=15): Mean Age=30.8yr; Gender: Male=9, Female=6; Mean GCS=10.8; Mean Time Post Injury=3.8yr. **Intervention:** Patients were randomized into the GMT or MST group. The GMT was comprised of five steps: 1) orienting and alerting to task, 2) goal selection, 3) partitioning goals into sub-goals, 4) encoding and retention of sub-goals, and 5) monitoring. The MST was training that was unrelated to goal management: reading and tracing mirror-reversed text and designs. Participants were tested on everyday paper and pencil tasks that focused on holding goals in mind, sub-goal analysis and monitoring. **Outcome Measures:** Goal Neglect (Everyday paper and pencil tasks), Stroop Interference Procedure, Trail Making A and B, Wechsler Adult Intelligence Scale Revised (WAIS-R).	Everyday paper and pencil Task 1. The GMT group compared to the MST group had significantly greater accuracy on the everyday paper and pencil tasks post-training (p<0.05). 2. The MST group also had significantly more errors during the everyday paper and pencil tasks (p<0.01). 3. The GMT group significantly reduced their errors from pre-post training during the everyday paper and pencil tasks (p<0.01). 4. The GMT also devoted significantly more time to proofreading and the room-layout tasks than the MST group from pre to post-training (p<0.05). Neuropsychological Tasks 1. The GMT group was generally slower on timed neuropsychological tests: Stroop Interference Procedure, Trail Making Part A and B (p<0.05 and p<0.06, respectively). 2. No significant differences between groups for the WAIS-R (p>0.05).
Sohlberg et al. (2000) USA RCT PEDro=8 N=14	**Population:** TBI=11, ABI=1, Other=2. *Attention Process Training (APT) Group (n=7)*: Mean Age=33.1yr; Mean Time Post Injury=7.5yr; *Control Group (n=7)*: Mean Age=38.1yr; Mean Time Post Injury=1.6yr. **Intervention:** Patients were randomized to receive either the APT training (treatment) or the brain injury education and supportive listening (control), in a cross over design. APT was 24hr over 10wk and the control group received 10hr over 10wk. All subjects worked directly with a therapist and assessed pre and post intervention. **Outcome Measures:** Trail Making Test, Paced Auditory Serial Addition Task (PASAT), Gordon Diagnostic Vigilance and Distraction, Controlled Oral Word Association Task (COWAT), Stroop Task, Attention Questionnaire.	1. Those in the APT group reported significantly more changes than the control group (0.91 and 0.58 respectively, p<0.05). 2. The effect of type of change was significant (p<0.0001); a greater number of memory/attention changes were reported for the APT group, whereas more psychological changes were reported for the control. 3. Changes in PASAT scores corresponded with perceived cognitive improvement in the interview; changes in PASAT scores were greater for those who reported >2 cognitive changes (p<0.05). 4. Results of the PASAT, Stroop Task, Trail Making Test B, and COWAT also found that those with higher levels of vigilance had improved scores (p<0.01). 5. For the aforementioned tasks, there were also specific improvements in performance associated with APT that were greater than those associated with brain injury education (p<0.05).

[Fasotti et al.](#) (2000) Netherlands RCT PEDro=5 N=22	**Population:** TBI; *Experimental Group (n=12)*: Mean Age=26.1yr; Gender: Male=8, Female=4; Mean Time Post Injury=9.8mo. *Control group (n=10)*: Mean Age=30.1yr; Gender: Male=7, Female=3; Mean Time Post Injury=8.3mo. **Intervention:** Patients in the experimental group received Time Pressure Management (TPM) training (1hr, 2-3x/wk, 2-3wk). TPM training used videotaped short stories. The program was designed to increase awareness of errors and deficits, encourage the acceptance and acquisition of the TPM strategy, and emphasize strategy application and maintenance. The control group received concentration training (30min, 2-5hr/wk, 3-4hr). Mean training was 7.4hr and 6.9hr for the TPM and control groups, respectively. Patients were assessed 2wk prior to training, post-training, and at 6mo follow-up. **Outcome Measures:** Waterbed (WB) and Harvard Graphics (HG) tasks, Rey's 15-word test, Rivermead Behavioural Memory Test, Auditory Concentration Test, Paced Auditory Serial Addition Task, Visual Choice Reaction Time Task.	1. Training improved performances in both HG and WB tasks, but differences were not significant relative to control. 2. Scores on 2 of 3 standardized memory variables and all 3 attention variables increased significantly in the TPM group (p<0.05), whereas no memory variables and 1 of 3 attention variables increased significantly for the control group. 3. Follow-up (6 mo) data for 10 from the TPM group and 9 from the control group indicated that there was a significant time effect (p<0.05) but no significant group time interaction (p=0.23); this suggests that there still was a significant improvement after 6 mo but that this improvement could not be attributed specifically to the treatment or control training.
[Niemann et al.](#) (Niemann et al., 1990) (1990) United States RCT PEDro=7 N=29	**Population:** *Attention Group (N=13)*: Mean age=28.9yr; Mean time post-injury=41mo. *Memory Group (N=13):* Mean age=34.3yr; Mean time post-injury=37.1mo. **Intervention:** Individuals were randomly assigned to either an attention training program or a memory training program. Both programs lasted 9 weeks and had two 2-hour sessions each week. **Outcomes:** Attention Test d2, Paced Auditory Serial-Addition Task (PASAT), Divided Attention test (DAT), Trail Making Test-B (TMT-B), Rey Auditory Verbal Learning Test (RAVLT), Block Span Learning Test (BSLT), Ruff 2 & 7 Test, Logical Memory Subtest (Wechsler Memory Scale) (WMS-LM), Ruff-Light Trail Learning Test (RLTLT).	1. There were no significant within-group differences on the Test d2, PASAT, DAT, RAVLTBSLT, Ruff 2 & 7 Tests, WMS-LM, or the RLTLT. 2. Significant within group differences were seen on the TMT-B for both the attentional (p<0.01), and memory (p<0.01) groups. 3. The attention group improved significantly more on the TMT-B compared to the memory group (p=0.05). 4. The attention group improved significantly more than the memory group on the Attention Test d2 (p=0.02). 5. No other significant differences were found.
[Bosco et al.](#) (2018) Italy Pre-post N=19	**Population:** *Severe TBI:* Mean age=38.5yr; Gender: Male=16, Female=3; Mean time post-injury=99.4 months; GCS<8. **Intervention:** Groups of 5-6 participants met twice a week for 12 weeks for a total of 24 Cognitive Pragmatic Treatment (CPT) sessions. Participants were assessed at four time points, 3-months pretreatment, immediately before treatment, immediately following treatment, and 3-months post-treatment. **Outcome Measures:** Assessment Battery for Communication (ABaCo), Communications Activities of Daily Living (CADL), Aachener Aphasie test, Attentional Matrices, Trail Making test, Verbal Span, Corsi's Block-Tapping test, immediate and deferred recall test, Tower of London test, Modified Card Sorting test, Raven Colored Progressive Matrices, Sally & Ann, Strange Stories.	1. There was a significant difference in scores on the ABaCO between pretreatment and posttreatment scores (p<0.001). There were no significant differences between the two initial time points or the two posttreatment timepoints. 2. Similar results were seen for the CADL, with individuals showing a significant improvement in their functional communication skills following treatment (p=0.024). 3. Between immediate pretreatment scores and immediate posttreatment scores significant differences were only seen on the Verbal Span (p=0.045), and the Modified Card Sorting test (p=0.004).

Hellgren et al. (2015) Sweden Case Series N=48	**Population:** Cerebral infarction=23%, TBI=21%, Infection=19%, Intracerebral hemorrhage=13%, Subarachnoid hemorrhage=10%, Brain tumor=8%, Other=6%; Mean Age=43.7yr; Gender: Male=30, Female=18; Mean Time Post Injury=51.2mo. **Intervention:** Participants received a working memory training program (Cogmed) consisting of various visuospatial and verbal working memory tasks. There were 4-5 sessions/wk for 5-7wk, consisting of 45-60min of intense exercise with one break. Occupational therapist coaches were present during every session and provided weekly feedback in addition to continuous feedback from the computer program. **Outcome Measures:** Paced Auditory Serial Attention Test (PASAT 2.4), Forward and backward block repetition, Listening Span Task, Canadian Occupational Performance Measure (COPM performance and satisfaction), EuroQol descriptive (EQ-5D Index), EuroQol visual analogue scale (EQ-VAS), Working Memory Index (WM Index).	1. At 20wk post-training, there were significant improvements in PASAT ($p<0.001$), Listening Span ($p<0.001$), Forward block repetition ($p<0.001$), Backward block repetition ($p<0.001$), COPM performance ($p<0.001$), COPM satisfaction ($p<0.001$), EQ-5D index ($p=0.009$), and EQ-VAS ($p<0.001$) compared to baseline. 2. Compared to baseline, all participants significantly improved their WM Index at 20wk follow-up ($p<0.001$). 3. No significant differences in treatment effect were found for all outcomes in terms of sex or time post-injury, except for ≤18 mo since injury exhibiting more improvement than >18mo in terms of WM index difference ($p<0.05$), COPM performance improvement ($p<0.05$), and COPM satisfaction improvement ($p<0.05$).
Serino et al. (2007) Italy Case Series N=9	**Population:** TBI: Age range=16-57 yr; Gender: male=6, female=3; Time since injury=6-78 months. **Intervention:** A long sequence of numbers is presented, and patients were asked to add each new number to the number preceding it and say the sum out loud. Two additional tests (the Months tasks and the Word tasks) were also administered in a similar way. The GST and the WMT were each 4 sessions/week, for 4 weeks. To vary tasks and their level of difficulty, in the interstimulus interval was varied. **Outcome Measures:** Working memory training (WMT); Paced Auditory Serial Addition Test (PASAT); Months task	1. Study results indicate the greatest improvement in performance occurred from the intermediate to the final sessions ($p<0.0005$) after the WMT. 2. Improvement from the initial to intermediate sessions did not show any significant improvement in working memory ($p<0.46$) after GST. 3. Working memory ($p<0.05$), divided attention ($p<0.05$), executive function ($p<0.05$), and long-term memory ($p<0.05$) for subjects were significantly improved in the final session compared to the intermediate session. 4. The same was not noted on the speed processing and sustained attention tasks ($p>0.05$). Working memory training tasks were also found to improve scores on various psychosocial outcomes.
Boman et al. (2004) Sweden Pre-Post N=10	**Population:** TBI: Mean age=47.5yr; Gender: male=5, female=5; Time Post injury=9-40 months. **Intervention:** Each participated in an individual cognitive training session for 1 hr/3x a week for 3 weeks at home or work. The program included attention process training (APT), generalization for training and teaching of compensatory strategies for self-selected cognitive problems. Identification of cognitive problems in everyday life was also part of the compensatory strategy. **Outcome Measures:** Digit Span Test; Claeson-Dahl test; Rivermead Behavioural Memory test (RBMT); Assessment of Motor and Process Skills; European Brain Injury Questionnaire.	1. For the following: sustained attention, selective attention and alternating attention significant changes ($p<0.05$, $P<0.05$, $p<0.01$ respectively) were noted in the scores of the APT test and Digit Span task between the pre to post training session and the 3 mo follow up. 2. Score increases ($p<0.05$) on the RMBT were found at the 3 mo follow up compared to the RMBT scores at the pretest. 3. When looking at changes in the RBMT score pre to post training, changes were not found. 4. No significant changes were found (pre to post and pre to 3 mo follow up) when looking at the scores on the Claeson-Dahl Memory

Park et al. (1999) Canada Case-Control N=46	**Population:** TBI=23; Age matched controls=23. **Intervention:** Attention process training program of 20 two-hour sessions for a total of 40 hr. **Outcome Measure:** Paced Auditory Serial Addition Task (PASAT); Consonant Trigrams; Beck Depression Inventory (BDI).	1. No statistically significant improvements on the BDI from pre- to post-treatment for the TBI group. 2. TBI (p<0.01) and control (p<0.001) groups improved significantly in PASAT before/after tests. 3. Performance declined with increases in delay (p<0.001), and study position (p<0.001) on the Consonant trigrams.

Discussion

Many studies examined the effects goal training or cognitive training (Boman et al., 2004; Chen et al., 2011{Novakovic-Agopian, 2011 #26; Laatsch et al., 1999; Novakovic-Agopian et al., 2011; Sohlberg et al., 2000). Levine et al. (2000) completed an RCT comparing patients using goal management training strategies to a control group exposed to only motor skills training. The treatment group improved on paper and pencil everyday tasks as well as meal preparation, which the authors used as an example of a task heavily reliant on self-regulation. Novakovic-Agonian et al. (2011), found similar results in an RCT crossover where participants were assigned to received goal-training followed by education or the reverse. The goal training first group saw a significant improvement in sustained attention compared to the education-first group, additionally the goal training first group maintained their gains over 10 weeks.

A more recent RCT (Dundon et al., 2015) examined the effect of adaptive training on dichotic listening tasks and attention, interestingly the adaptive training group had significantly higher scores on the listening task compared to non-adaptive training group; however, the non-adaptive training group surpassed the adaptive training group in Test of Everyday Attention (TEA) scores. Overall, both groups significantly improved on measures of attention as a result of time (Dundon et al., 2015).

Park et al. (1999) examined whether Attention Processing Training (APT) had a beneficial effect on attention measures (PASAT, Consonant Trigrams) in a group with severe TBI (tested pre and post training approximately 7 months apart). They compared their results to a convenience sample of controls, given the same measures one week apart without training. Results suggested that the APT did not have a significantly beneficial effect as performance improved on all measures across both groups (indicating practice effects and possibly spontaneous recovery). A pre-post study (Boman et al., 2004) found that cognitive training for three weeks significantly improved attention task scores compared to pre-test scores. One study did demonstrate that cognitive training (although beneficial) may not be more beneficial than other interventions such as educational training with respect to processing speed (Chen et al., 2011). In this study both groups significantly improved in attention directed goal completion.

Another study comparing the effects of attentional training to physical exercise found that there was no significant difference between groups post-intervention, but there was a within subjects effect such that both groups reported significantly less cognitive failures (McMillan et al., 2002). Attention process training, was also shown to have greater results in attention remediation compared to education alone (Sohlberg et al., 2000). One study examined the effects of a memory training program on attention and reported positive results; Hellgren et al. (2015) found that a memory training program was successful in improving attentional scores on the Paced-Auditory Serial Attention Test, as well as further enhancing memory in general which is discussed later in this chapter.

In a study directly comparing the effects of an attention training program with that of a memory training program, the authors found that the results were split, with individuals performing better on some measures of attention (Attention Test 2d) but not others (PASAT) (Neiman et al., 1990). The last study to use an attention training program sought to see if the presence of a therapy animal could enhance the effects of training (Gocheva et al., 2018). Both the animal therapy and non-animal therapy groups produced significant improvement on measures of attention and concentration; however, the animal therapy group had a significantly larger increase in concentration (Gocheva et al., 2018).

Emotional regulation was also examined as a potential intervention for the remediation of attention postABI (Cantor et al., 2014). However, this treatment was not seen to be effective in the recovery of attention, other significant effects on executive functioning from this study are discussed further in section 6.4.1.1. Another study which focused specifically on mindfulness (McHugh & Wood, 2013) found that mindful focused training significantly improved participants's ability to correctly select stimuli compared to controls.

Fasotti et al. (2000) assessed the effectiveness of time pressure management (TPM) training compared to concentration training in patients with slowed processing speed as a result of traumatic brain injury. Though both groups showed improvements on information intake task performance, no significant differences between groups were observed even though specific time pressure management strategies were learned by the experimental group (Fasotti et al., 2000). "Cognitive pragmatic treatment' has been found to significantly improve scores on the card sorting task; however, the specific details of this program were not stated (Bosco et al., 2018b).

The inconsistencies between studies may be due to a lack of standardized goal management training or attention process training protocols. The lack of a consensus on the definition of certain cognitive processes appears to be reflected in the interventions used to attempt to rehabilitate these deficits. Unfortunately, this decreases the ability to compare studies on a more specific level; however, general conclusions can still be made that specific training programs which intend to increase attentional capacity are effective, to what extent they are more beneficial than other training programs needs to be addressed in the future through comparative methodologies. Only one study (Serino et al., 2007) described the specific task that was successful in improving attention. This cognitive task involved mental addition in combination with two other standardized tasks and was an effective strategy for improving attention.

Conclusions

There is level 2 evidence that adaptive training is no more effective than non-adaptive training in remediating attention in ABI populations.

There is level 1b evidence that emotional regulation therapy is not effective in treating attentional disorders compared to waitlist controls in ABI populations.

There is level 1b evidence that the addition of a therapy animal to attention training programs may enhance gains in concentration in those with an ABI.

There is level 2 evidence that mindfulness training compared to no intervention may improve an individual's ability to correctly reject inappropriate stimuli post ABI.

There is level 2 evidence to suggest goal management training, when compared to education, may be effective at improving attention in individuals post ABI.

There is level 2 evidence that goal management training is more effective in remediating task completion times than motor skill training, however it is not more effective in treating attention deficits, in individuals post ABI.

There is conflicting (level 2) evidence that attentional control or processing training may not significantly improve attention in post ABI individualscompared to control training.

There is level 4 evidence that summation tasks may be effective at improving attention in individuals post ABI.

There is level 4 evidence that a working memory training program may remediate attention in individuals post ABI.

There is level 4 evidence that cognitive rehabilitation therapy may not be effective for improving attention post ABI.

Goal management training is effective in assisting those who sustain an ABI learning to manage life goals through improved attention.

In general, a variety of non-specific attentional training programs appear to be effective for improving attentional scores following an ABI.

The addition of a therapy animal to an attentional training program may enhance concentration gains.

Therapies which focus on emotional regulation do not appear to be effective at improving attention post ABI, while mindfulness may improve some areas.

In order to determine if attentional training is effective in improving attention post-ABI standardized protocols must be developed to allow between study comparisons.

Tasks that involve mathematical skills may be effective at improving attention post ABI.

6.1.1.5 Brain Stimulation Techniques

Transcranial Direct Current Stimulation (tDCS) is a technique that painlessly delivers electrical currents to specific regions of the brain. These electrical currents modulate neuronal activity through electrodes placed over the head at different regions. Two recent studies have examined the effects of tDCS on attention post ABI.

Table 6.5 The Effect of Transcranial Direct Current Stimulation on Attention Post ABI

Author Year Country Research Design PEDro Sample Size	Methods	Outcome
Lee & Kim (2018) South Korea RCT PEDro=7 N=13	**Population:** *Experimental Group (N=7):* Mean age=42.42yr; Gender: Male=5, Female=2; Mean time post-injury=3.85 months; Mean GCS=13.71. *Control Group (N=6):* Mean age=41.33yr; Gender: Male=4, Female=2; Mean time post-injury=3.88 months; Mean GCS=13.66. **Intervention:** Individuals received either rTMS or sham rTMS for 30mins 5 times a week, for 2 weeks. **Outcomes:** Montgomery-Asberg Depression Rating Scale (MADRS), Trail Making Test (TMT), Stroop Color Word Test (SCWT).	1. The experimental group experienced significant within group differences on the MADRS ($p<0.05$), TMT ($p<0.05$), and SCWT ($p<0.05$). 2. No significant within group differences were seen for the control group. 3. Following intervention, the experimental group had significantly lower scores on the MADRS ($p<0.05$), TMT ($p<0.05$), and SCWT ($p<0.05$). *Lower scores indicate improved performance on TMT and SCWT.
Sacco et al. (2016) Italy RCT PEDro=4 N=32	**Population:** TBI. Mean Time Post Injury=8.73yr; Severity: Severe=32, Moderate=0, Mild=0. *Treatment Group (TG, n=16):* Mean Age=37.7; Gender: Male=12, Female=4. *Control Group (CG, n=16):* Mean Age=35.2; Gender: Male=14, Female=2. **Intervention:** Participants were randomized to receive transcranial direct current stimulation (tDCS, TG) or sham tDCS (CG) with computer-assisted training (2/d, 5d). Outcomes were assessed at baseline (T0), before treatment (T1), after treatment (T2), and 1-month follow-up (T3). **Outcome Measures:** Test for the Examination of Attention, Divided Attention subtest (DA); Repeatable Battery for the Assessment of Neurological Status (RBANS).	1. For DA, the TG performed significantly better at T2 compared to T0 and T1, with faster reaction times ($p=0.004$) and fewer omission errors ($p<0.0001$). 2. For DA, the CG did not perform better at T2 compared to T0 and T1. 3. For DA, there was a significant interaction between time (T0/T1 vs T2) and group (TG vs CG), for both reaction time ($p=0.05$) and omission errors ($p=0.03$). 4. On RBANS, the TG showed a non-significant improvement in performance on attention task ($p=0.057$), but no improvement on visual-spatial abilities, semantic fluency, working memory, and long-term memory.

Discussion

Two RCTs have examined brain stimulation techniques to improve attention following an ABI (Lee & Kim, 2018; Sacco et al., 2016). Only Sacco et al. 2016 examined the effects of transcranial direct current stimulation (tDCS) on attention in a population post ABI. The authors found that the addition of transcranial direct current stimulation to computer-assisted training was superior to sham stimulation for improving divided attention. However, more high-level studies are needed in order to fully examine the potential benefits of adding tDCS to traditional attentional therapies. The second study examined the effects of repetitive transcranial magnetic stimulation (rTMS), and found significant positive effects on attention and depression when compared to sham controls (Lee & Kim, 2018).

There is level 2 evidence that transcranial direct current stimulation when combined with an attention training program (compared to sham stimulation) may improve divided attention in individuals post ABI.

There is level 1b evidence that repeated transcranial magnetic stimulation compared to sham stimulation may improve attention following an ABI.

Transcranial direct current stimulation may be effective in remediating attentional deficits when combined with computer assisted training in ABI populations.

Repeated magnetic transcranial stimulation may be effective in remediating attentional deficits following an ABI.

6.1.2 Pharmacological Interventions

6.1.2.1 Donepezil

Donepezil, an acetylcholinesterase inhibitor, was originally developed for improving cognitive function and memory in people with Alzheimer's disease (Cacabelos, 2007), by delaying cognitive impairment in (Takeda et al., 2006). Since evidence suggests that cholinergic dysfunction may contribute to persistent cognitive deficits for people after traumatic brain injury, improvements in attention, memory, and other aspects of cognition related to the acetylcholine system are expected when cholinergic function is reduced (Arciniegas, 2003).

Table 6.6 The Effect of Donepezil on Memory and Cognitive Functioning Post ABI

Author Year Country Research Design PEDro Sample Size	Methods	Outcome
Zhang et al. (2004) USA RCT PEDro=7 N=18	**Population:** TBI; *Group A (n=9)*: Mean Age=33yr; Gender: Male=6, Female=3; Mean GCS=9.3; Mean Time Post Injury=4.6mo; *Group B (n=9)*: Mean Age=31yr; Gender: Male=7, Female=2; Mean GCS=8.9; Mean Time Post Injury=3.9. **Intervention:** In a randomized crossover trial, Group A received oral donepezil for the first 10wk, followed by a washout period of 4wk, then followed by 10wk of placebo. Group B received the treatments in the opposite order. Donepezil was administered at 5mg/d for the first 2wk, and at 10mg/d for the remaining 8wk. **Outcome Measures:** Auditory (AII) and Visual (VII) subtests of Wechsler Memory Scale-III, and the Paced Auditory Serial Addition Test (PASAT).	1. At week 10, Group A achieved significantly better scores in AII (95.4±4.5 versus 73.6±4.5; p=0.002), VII (93.5±3.0 versus 64.9±3.0; p<0.001), and in the PASAT (p≤0.001) compared to Group B. 2. This increase in scores in Group A were sustained after washout and placebo treatment (week 24), leading to no significant differences in AII (105.9±4.5 versus 102.4±4.5; p=0.588), VII (91.3±3.0 versus 94.9±3.0; p=0.397), and PASAT (p>0.1) compared to Group B at study end. 3. Within-group comparisons showed that patients in both Group A and Group B improved significantly in AII and VII (p<0.05), as well as in PASAT (p<0.001), after receiving donepezil.
Campbell et al. (2018) United States PCT N=129	**Population:** *Donepezil Group (N=55):* Mean Age=34.4yr; Gender: Male=80%, Female=20%; Mean time post injury=28.6d; Injury Severity=Moderate-severe. *Control Group (N=74)*: Mean Age=40.8yr; Gender: Male=71.6%, Female=28.4%; Mean time post injury=25.2d; Injury Severity=Moderate-severe. **Intervention:** Individuals were assigned to receive either donepezil or a placebo treatment for an average of 67.5 days. Those receiving donepezil started with a dosage of 5mg/day, increasing to 10mg/day over the course of 7-10 days. Follow-up	1. For both parts of the Trail Making Test (Part A and B), there was a significant effect of time (p<0.001, p<0.001) respectively. Demonstrating that both groups significantly improved over time. No other significant effects were found for the Trail Making Test. 2. Likewise, in the DS, only a significant effect of time (p<0.001) was observed. 3. For both the learning and memory components of the CVLT-II there was only a significant effect of time observed (p<0.001, p<0.001).

Author Year Country Research Design PEDro Sample Size	Methods	Outcome
	assessments took place approximately 61.4 days after treatment. **Outcome Measures:** Trail Making Tests (Part A and B), Digit Span index (DS), California Verbal Learning Test-II (CVLT-II), Logical Memory II (LMII), Functional Independence Measure (FIM), Disability Rating Scale (DRS).	4. The LMII showed similar results with only a significant effect of time observed (p=0.005). 5. For measures of disability, both the DRS and the FIM also only showed a significant effect of time for both groups respectively (p<0.001, p<0.001). 6. Overall, there were no significant effects of treatment found, however both groups did demonstrate significant spontaneous recovery.
Khateb et al. (2005) Switzerland Pre-Post $N_{initial}$=15, N_{final}=10	**Population:** TBI; Mean age=43yr; Gender: Male=8, Female=7; Mean Time Post Injury=42mo. **Intervention:** Patients were administered donepezil 5 mg/day for 1mo, followed by 10 mg/day for 2mos. **Outcome Measures:** Stroop test, Trail Making Test (TMT), Rey Auditory Verbal Memory Test (RAVMT) and Test for Attentional Performance (TAP).	1. 4 of 15 participants stopped due to side effects within the first week (e.g., nausea, sleep disorders, anxiety, dizziness, etc.). 2. Changes on the neuropsychological evaluation show modest improvement, the comparison of the global score of all questionnaires before and after therapy was marginally significant (p=0.058). 3. A significant improvement in executive function was only found for the Stroop Colour naming test (87.3±22.9 to 79.5±19.1, p=0.03); for learning and memory the RAVMT-learning (47.7±6.9 to 53.5±5.0, p=0.05); and for attention, the errors subsection of divided attention (5.8±3.3 to 2.9±2.7, p=0.03).

Discussion

In an RCT, Zhang et al. (2004) demonstrated that donepezil was associated with significantly more improvement in tasks of sustained attention compared to placebo. These improvements were sustained even after the washout period. Once both groups had completed donepezil treatment there were no significant differences between groups on any measures of attention. Khateb et al. (2005) found that individuals performed significantly better on measures of divided attention after donepezil treatment; however, 4 of 15 participants stopped treatment due to negative side-effects. In contrast to the positive effects found by these studies, one prospective controlled trial found no significant effects of donepezil on any measures of cognition, including attention (Campbell et al., 2018). In both the Campbell et al. (2018) and Zhang et al. (2004) studies, individuals received donepezil for approximately the same duration.

Conclusion

There is conflicting level 1b (positive) and level 2 (negative) evidence that donepezil may improve attention compared to placebo post ABI.

It is unclear as to whether donepezil may improve attention in individuals with a moderate to severe ABI.

6.1.2.2 Methylphenidate

Methylphenidate is a central nervous stimulant (CNS) which inhibits the reuptake of dopamine and norepinephrine, resulting in increased dopaminergic activity. In healthy individuals, methylphenidate has been found to improve memory but not other cognitive functions such as attention, mood, or executive function (Repantis et al., 2010). Methylphenidate is extensively used as a treatment for attention deficit disorder, as well as narcolepsy (Glenn, 1998). No serious side effects have been observed in clinical trials, though there is a lack of evidence for long term safety (Godfrey, 2009).

Table 6.7 The Effect of Methylphenidate on Attention, Concentration, and Processing Speed Post ABI

Author Year Country Research Design PEDro Sample Size	Methods	Outcome
Dymowski et al. (2017) Australia RCT PEDro=9 $N_{Initial}$=11, N_{Final}=10	**Population:** TBI. *Methylphenidate Group (n=6)*: Mean Age=35 yr; Gender: Male=4, Female=2; Mean Time Post Injury=366 d; Mean Worst GCS=4.83. *Placebo Group (n=4)*: Mean Age=32.5 yr; Gender: Male=2, Female=2; Mean Time Post Injury=183.5 d; Mean Worst GCS=4.50. **Intervention:** Participants were randomly assigned to receive either methylphenidate (0.6 mg/kg/d rounded to the nearest 5mg with maximum daily dose of 60 mg) or placebo (lactose). Outcomes relating to processing speed, complex attentional functioning, and everyday attentional behaviour were assessed at baseline, 7 wk (on-drug), 8 wk (off-drug), and 9mo follow-up. **Outcome Measures:** Symbol Digit Modalities Test (SDMT), Trail Making Test (TMT) A and B; Hayling (A, B, error), Digit Span (DS-Forward, Backward, Sequencing, Total), Ruff 2&7 Selective Attention Test Automatic Speed Raw Score (2&7 ASRS), Ruff 2&7 Selective Attention Test Controlled Speed Raw Score (2&7 CSRS), Simple Selective Attention Task Reaction Time (SSAT RT), Complex Selective Attention Task Reaction Time (CSAT RT), N-back 0-back RT, N-back 1-back RT, N-back 2-back RT, Rating Scale of Attentional Behaviour Significant Other (RSAB SO).	1. After applying Bonferroni corrections, no significant differences between groups from baseline to 7 wk, baseline to 8 wk, or baseline to 9 mo were observed for SDMT, TMT A, TMT B, Hayling A, Hayling B, Hayling error, DS Forward, DS Backward, DS Sequencing, DS Total, 2&7 ASRS, 2&7 CSRS, SSAT RT, CSAT RT, N-back 0-back RT, N-back 1-back RT, N-back 2-back RT, or RSAB SO.
Zhang and Wang (2017) China RCT PEDro=10 $N_{Initial}$=36, N_{Final}=33	**Population:** TBI; Severity: mild to moderate. *Methylphenidate Group (n=18)*: Mean Age=36.3 yr; Gender: Male=13, Female=5. *Placebo Group (n=18)*: Mean Age=34.9 yr; Gender: Male=14, Female=4. **Intervention:** Participants were randomly assigned to receive methylphenidate (flexibly titrated from 5 mg/d at the beginning, then gradually increased by 2.5 mg/d until reaching 20 mg/d) or placebo for 30 wk. **Outcome Measures:** Mental Fatigue Scale (MFS), Choice Reaction Time (CRT), Compensatory Tracking Task (CTT), Mental Arithmetic Test (MAT), Digit Symbol Substitution Test (DSST), Mini-Mental State Examination (MMSE), Beck Depression Inventory (BDI), Hamilton Rating Scale for Depression (HAMD).	1. At baseline, there were no significant differences between groups in terms of demographics, MFS, CRT, CTT, MAT, DSST, MMSE, BDI, or HAMD. 2. Post-intervention, the experimental group had significantly lower scores compared to control group for MFS (p=0.005), CRT (p<0.001), CTT (p<0.001), BDI (p=0.040), and HAMD (p=0.005). 3. Post-intervention, the experimental group had significantly higher scores compared to control group for MAT (p=0.020), DSST (p<0.001), MMSE (p<0.001).

Author Year Country Research Design PEDro Sample Size	Methods	Outcome
Willmott et al. (2013) Australia RCT PEDro=10 N=32	**Population:** TBI; Gender: Male=21, Female=11; Mean Time Post Injury=68 d; *TBI Val/Val Group (n=11)*: Mean Age=22.64 yr; Mean GCS=4.67; *TBI Val/Met Group (n=14)*: Mean Age=28.57 yr; Mean GCS=5.38; *TBI Met/Met Group (n=7)*: Mean Age=30.57 yr; Mean GCS=6.83. **Intervention:** Participants with TBI, in a crossover design, received 0.3 mg/kg methylphenidate (2 ×/d) for 6 sessions in total (spanning 2 wk), alternating between treatment and placebo for every other session. Results were compared against those from healthy controls (n=40). Groups were stratified by the presence of the Val158Met gene. **Outcome Measures:** Ruff 2 & 7 Selective Attention Test – automatic (2 & 7 ASRS) and controlled (2 & 7 CSRS), Selective Attention Task, Four Choice Reaction Time Task (4CRT) – dissimilar compatible (DC) and similar incompatible (SI), Symbol Digit Modalities Test (SDMT), Letter Number Sequencing Task, Wechsler Test of Adult Reading.	1. At baseline, there were no significant differences across various genotypes on attentional performance. 2. Participants with TBI and Met/Met alleles performed significantly poorer on the SDMT (p<0.0005), 2 & 7 ASRS (p=0.001), 2 & 7 CSRS (p<0.0005), DC RT (p=0.005), and SI RT (p=0.002), when compared to controls. Analyses with participants with TBI and Val/Val alleles showed even worse outcomes, demonstrating poorer performance on 7/8 outcome measures. 3. Following methylphenidate treatment one significant drug and genotype interaction was seen between Met/Met carriers and performance on the SDMT (F=4.257; p=0.024), suggesting Met/Met carriers were more responsive to methylphenidate than either of the others.
Kim et al. (2012) USA RCT PEDro=7 N=23	**Population:** Moderate/Severe TBI; Mean Age=34.2 yr; Gender: Male=18, Female=5; Mean Time Post Injury=51.1 mo. **Intervention:** In a crossover design, participants were randomly assigned to receive 0.3 mg/kg methylphenidate followed by placebo, or the reverse and were assessed after each. **Outcome Measures:** Visual sustained attention task (VSAT), Two-back task.	1. Relative to placebo, both accuracy (1.62±1.03 versus 2.23±1.07; p<0.005) and mean reaction time (827.47±291.17s versus 752.03±356.87s; p<0.050) in the VSAT were improved significantly on MPH. 2. Relative to placebo, mean reaction time (929.31±192.92s versus 835.02±136.12s; p<0.050), but not accuracy, in the two-back task was improved significantly when on MPH.
Willmott & Ponsford (2009) RCT PEDro=10 N=40	**Population:** TBI; Mean Age=26.93 yr; Gender: Male=28, Female=12; Time since injury=68.38 d. **Intervention:** Patients received either methylphenidate (0.3 mg/kg 2 x/d, rounded to the nearest 2.5 mg) or a placebo. Patients were seen for 6 sessions across 2-week period. Patients then crossed-over. **Outcome Measures:** Ruff 2 and 7 Selective Attention Test, Selective Attention Task, Four Choice Reaction Time Task, Sustained Attention to Response Task, Symbol Digit Modalities Test, Letter Number Sequencing Task, Wechsler Test of Adult Reading.	1. Methylphendiate significantly increased speed of information processing on the Symbol Digit Modalities Test (p=0.020); Ruff 2 and 7 Test-Automatic Condition (p=0.003); Simple Selective Attention Task (p=0.001); Dissimilar compatible (p=0.003), and Similar Compatible (p=0.002).
Kim et al. (2006) Korea RCT PEDro=6 N=18	**Population:** TBI; *Methylphenidate Group (n=9)*: Mean Age=30.1 yr; Gender: Male=9, Female=0; Mean Time Post Injury=1.6 yr; *Placebo Group (n=9)*: Mean Age=38.3 yr; Gender: Male=7, Female=2; Mean Time Post Injury=3.6 yr. **Intervention:** Patients were randomly allocated to receive either 20 mg methylphenidate or the placebo. Assessments were done at baseline (T1), 2 hr post treatment (T2), and 2 d later (T3). **Outcome Measures:** Visual sustained attention task (VSAT), Two-back task.	1. At T1 there were no significant differences in mean reaction time or in accuracy between the two groups. 2. For those in the treatment group, the mean reaction time of the two-back task improved significantly compared to those in the placebo group from T1 to T2 (13.74±13.22% versus 4.02±9.48%; p<0.05).

Author Year Country Research Design PEDro Sample Size	Methods	Outcome
		3. No significant difference in improvement as seen with accuracy of the two-back task (p=0.07), nor with the VSAT.
Whyte et al. (2004) USA RCT PEDro=8 N=34	**Population:** TBI; Mean Age=37 yr; Gender: Male=29, Female=5; GCS<12; Median Time Post Injury=3.2 yr. **Intervention:** Participants received 0.3 mg/kg/dose methylphenidate for 3 wk, 2×/d, and placebo for 3 wk, for a total of 6 wk, with conditions alternating weekly. Washout lasted a day, after which time the groups crossed over. **Outcome Measures:** Attention Tasks.	1. Methylphenidate showed significant improvements in information processing speed (p<0.001), work task attentiveness (p=0.010), and caregiver attention ratings (p=0.010), pre-post. 2. No treatment-related improvements were observed in susceptibility to distraction and divided or sustained attention.
Plenger et al. (1996) USA RCT PEDro=5 N=23	**Population:** TBI; Gender: Male=17, Female=6; *Placebo Group (n=13)*: Mean Age=26.6 yr; Mean GCS=8.1; *Methylphenidate Group (n=10)*: Mean Age=31.4 yr; Mean GCS=9.3. **Intervention:** Patients were randomly allocated to receive either methylphenidate or placebo. Methylphenidate was administered at 30 mg/kg, 2×/d, for 30 d. **Outcome Measures:** Disability Rating Scale (DRS), Continuous Performance Test (CPT), 2 & 7 Test (2 & 7), Paced Auditory Serial Addition Test (PASAT), Digit Span & Attention/ Concentration from Wechsler Memory Scale-Revised (Attn/Conc from WMS-R).	1. At 30 d follow-up (n=15), significant differences were obtained on DRS, suggesting better outcome for the methylphenidate group. This difference however was not seen at 90 d follow-up (n=11). 2. Significant differences were found on the attention-concentration domain at the 30 d follow-up, as indicated by CPT, PASAT, 2 & 7, and Attn/Conc from WMS-R (p<0.030). The treatment group performed better in these measures compared to the placebo group.
Speech et al. (1993) USA RCT PEDro=7 N=12	**Population:** TBI; Mean Age=27.6 yr; Gender: Male=5, Female=7; Mean Time Post Injury=48.5 mo. **Intervention:** In a crossover design, participants were randomly assigned to receive 0.3 mg/kg methylphenidate, 2 ×/d, for 1 wk, followed by 1 wk of placebo, or receive the treatment in the reverse order. **Outcome Measures:** Gordon Diagnostic System, Digit Symbol and Digit Span subtests of the Wechsler Adult Intelligence Scale-Revised, Stroop Interference Task, Sternberg High Speed Scanning Task, Selective Reminding Test, Serial Digit Test, Katz Adjustment Scale.	1. No significant differences were found between methylphenidate and placebo condition in any of the outcome measures studied.
Gualtieri & Evans (1988) United States RCT Crossover PEDro=7 N=15	**Population:** Mean age=24.1yr; Gender: Male=10, Female=5; Mean time post-injury=46.8mo. **Intervention:** Participants were assigned to receive three conditions in randomized order. 1) Placebo; 2) Methylphenidate (0.15mg/kg) twice daily; 3) Methylphenidate (0.30mg/kg) twice daily. Each condition was 12 days long, with 2 days washout between conditions. **Outcomes:** Adult Activity Scale self-administered (AAS-S), Adult Activity Scale (administrator)(AAS-O), Examiner's Rating Scale (EXRS), Self Rating Scale (SRS), Verbal Fluency Test (VFT), Non-verbal Fluency test (NVFT).	1. There was a significant improvement in AAS-S and AAS-O scores between the placebo and high-dose conditions (p<0.05). 2. There was a significant difference in SRS scores between the placebo group and the high-dose condition (p<0.05). 3. On the EXRS there was a significant difference between baseline and low-dose (p=0.012), placebo and low-dose (p=0.025), baseline and high-dose (p=0.012), with higher doses of methylphenidate having improved effects. 4. There was a significant improvement in VFT scores between baseline and the high-dose groups (p=0.017).

Author Year Country Research Design PEDro Sample Size	Methods	Outcome
		5. There was a significant difference on NVFT scores between baseline and placebo (p=0.008), baseline and low-dose (p=0.008), baseline and high-dose (p=0.008), and the placebo and high-dose group (p=0.018), with methylphenidate improving scores.
Whyte et al. 1997 United States RCT Crossover PEDro=7 N=19	**Population:** Mean age=30.7yr; Gender: Male=15, Female=4; Mean GCS=5.83. **Intervention:** Individuals were randomly assigned to either receive methylphenidate first or placebo, and then the reverse. Methylphenidate was given twice a day at a dose of 0.25mg/kg. **Outcomes:** Sustained arousal task, phasic arousal task, distraction task, choice reaction-time task, behavioral inattention.	1. There was a significant drug x performance interaction (p<0.001), where performance was differentially impacted by the drug on each assessment. 2. Group stratification revealed that methylphenidate was more effective for improving performance on attentional measures for younger participant than older ones (p<0.05). 3. There were no other significant effects.
Pavlovskaysa et al. (2007) Pre-Post Israel N=6	**Population:** TBI; Age Range=18-47 yr; Gender: Male=4, Female=2; GCS ≥8. **Intervention:** Participants were administered 5 to 10 mg of methylphenidate (MHP) over a 2-week period. Participants were evaluated before, during and after the administration of methylphenidate. **Outcome Measure**: Performance on the Visual Spatial Attention Task Analyzing Rightward and Leftward Shifts of Attention.	1. Prior to treatment, patients were found to have great difficulty in shifting attention between hemifields. 2. There was a significant improvement in the asymmetry with MHP (p<0.001). 3. The right-side performance was significantly better on average than the left side (0.77 versus 0.59; p<0.050). 4. Performance was significantly better for ipsilateral valid cueing (p<0.010) than for invalid cross-trials (p<0.001). 5. The difference between ipsi- and cross-cueing for left side target performance is significant for each of the stages (p<0.001).

PEDro=Physiotherapy Evidence Database rating scale score (Moseley et al., 2002a).

Discussion

The majority of studies evaluating the efficacy of methylphenidate have been RCTs. In an RCT, Whyte et al. (2004) indicated that speed of processing, attentiveness during individual work tasks and caregiver ratings of attention were all significantly improved with methylphenidate treatment. No treatment related improvement was seen in divided or sustained attention, or in susceptibility to distraction. Similarly, Plenger et al. (1996) and Pavlovskaysa (2007) found that methylphenidate significantly improved attention and concentration, and visuo-spatial attention, respectively. More recently, Kim et al. (2012) found that reaction time improved significantly while on the methylphenidate. This is in line with Willmott and Ponsford (2009) who found that administering methylphenidate to a group of patients during inpatient rehabilitation significantly improved the speed of information processing. A variety of studies with different dosing regimens and durations have found positive effects of methylphenidate (Gualtieri & Evans, 1988; Whyte et al., 1997; Zhang et al., 2004).

Speech et al. (1993) conducted a double blind placebo controlled trial evaluating the effects of methylphenidate following closed head injury. In contrast to the results noted by Whyte et al. (2004) and Plenger et al. (1996), methylphenidate did not demonstrate significant differences compared to placebo on measures of attention, information processing speed, or learning. Kim et al. (2006) examined the effects of a single-dose treatment of methylphenidate and, although a trend was found in favour of improved working and visuospatial memory for the treatment group, these results did not reach statistical significance. Conflicting results continue to be reported, as two high-quality RCTs reached different conclusions regarding methylphenidate use. While Dymowski et al. (2017) noted no improvements in any measures of attention and mental processing, Zhang et al. (2017) noted improvements in reaction time, arithmetic tests, and even mental health outcomes after intervention by methylphenidate.

A potential explanation for these conflicting results is proposed by Willmott et al. (2013). The authors hypothesized that an individuals' response to methylphenidate depends on their genotype. More specifically, that individuals possessing the methionine (Met) allele at the catechol-O-methyltransferase (COMT) gene would confer greater response to methylphenidate compared to those with the valine (Val) allele. While both Met/Met and Val/Val carriers performed more poorly in various attentional tasks compared to healthy controls, Met/Met carriers did show greater improvements in strategic control in attention than Val/Val carriers. As well, the authors were able to identify one significant drug and genetic interaction between Met/Met carriers and performance on the Symbol Digit Modalities Test (SDMT). These findings suggest Met/Met carriers may in fact be more responsive to methylphenidate than individuals with the Val genotype. However, further studies are needed to draw firm conclusions.

Conclusions

There is conflicting level 1a evidence regarding the effectiveness of methylphenidate following brain injury for the improvement of attention and concentration in individuals post ABI.

There is level 1a evidence that methylphenidate improves reaction time of working memory compared to placebo in individuals post ABI.

There is level 1b evidence that individuals carrying the Met allele may be more responsive to methylphenidate than those without the Met allele when it comes to the ABI population.

The effectiveness of methylphenidate treatment to improve cognitive function following brain injury is unclear.

Methylphenidate may be effective in improving reaction time for working memory.

Response to methylphenidate may depend on the presence of the Met genotype.

6.1.2.3 Bromocriptine

Bromocriptine is a dopaminergic agonist which exerts its effects primarily through the binding of D_2 receptors (Whyte et al., 2008). It has been suggested that dopamine is an important neurotransmitter for prefrontal function (McDowell et al., 1998). In a study looking at the effects of bromocriptine on rats, Kline et al. (2002) noted that the animals showed improvement in working memory and spatial learning;

however, this improvement was not reflected in motor abilities. Two studies have been identified investigating the use of bromocriptine as an adequate treatment for the recovery of cognitive impairments following brain injury.

Table 6.8 The Effect of Bromocriptine on Attention Post ABI

Author Year Country Research Design PEDro Sample Size	Methods	Outcome
Whyte et al. (2008) USA RCT PEDro=7 N=12	**Population**: Moderate/ Severe TBI; Mean Age=35.75 yr; Gender: Male=8, Female=4; Median Time Post Injury=3.3 yr. **Intervention:** In a crossover design, participants were randomly assigned to receive bromocriptine (1.25 mg 2×/d titrated to 5mg 2×/d over a 1 wk), followed by placebo or the reverse order. Each lasted 4 wk with a 1 wk washout period. **Outcome Measures:** Attention Tasks.	1. Though some improvements were observed in certain subtests of attentional tasks (e.g. speed decline, decline in responding, test of everyday attention), they were not significant. 2. Overall results suggest bromocriptine had little effect on attention.
McDowell et al. (1998) USA RCT PEDro=4 N=24	**Population:** TBI; Median Age=32.5 yr; Gender: Male=20, Female=4; GCS Range=3-8; Time Post injury Range=27d-300 mo. **Intervention:** In a crossover design, participants were randomly assigned to receive 2.5 mg bromocriptine followed by placebo, or the reverse order. **Outcome Measures:** Dual-task paradigm (counting and digit span), Stroop Test, spatial delayed-response task, Wisconsin Card Sorting Test (WCST), reading span test, Trail Making Test (TMT), controlled oral word association test (COWAT), Control tasks.	1. Following bromocriptine treatment there were significant improvements on the dual-task counting (p=0.028), dual-task digit span (p=0.016), TMT (p=0.013), Stroop Test (p=0.05), COWAT (p=0.02), and WCST (p=0.041). 2. Bromocriptine had no significant effects on working memory (e.g. spatial delayed-response task and reading span test; p=0.978), or on control tasks (p=0.095).

PEDro=Physiotherapy Evidence Database rating scale score (Moseley et al., 2002a).

Discussion

The question of whether bromocriptine improves cognitive function in patients with ABI was explored in two RCTs (McDowell et al., 1998; Whyte et al., 2008). In an earlier investigation, low-dose bromocriptine (2.5 mg daily) improved functioning on tests of executive control including a dual task, Trail Making Test, the Stroop test, the Wisconsin Card Sorting Test and the controlled oral word association test (McDowell et al., 1998). However, bromocriptine did not significantly influence working memory tasks. However, a later study by Whyte et al. (2008) found that bromocriptine had little effect on attention and it was noted that several participants did experience moderate to severe drug effects and withdrew or were withdrawn from the study.

Although McDowell et al. (1998) demonstrated some benefits following administration of bromocriptine, there was only a single administration of bromocriptine and the dose was considerably lower than that given by Whyte et al. (2008). Spontaneous recovery may have been a factor leading to the improved abilities in individuals receiving a single dose (2.5 mg daily) of the medication; however, study results did not answer this question. Results from Whyte et al. (2008) noted that the placebo group demonstrated better (although not significant) trends in improvement on the various tasks administered.

Conclusions

There is conflicting evidence as to whether bromocriptine improves performance on attention tasks compared to placebo in patients post TBI.

Bromocriptine does not appear to improve attention in those with an ABI.

6.1.2.4 Cerebrolysin

Cerebrolysin has been demonstrated to have neuroprotective and neurotrophic effects and has been linked to increased cognitive performance in an elderly population. As explained by Alvarez et al. (2003), "*Cerebrolysin (*EBEWE Pharma, Unterach, Austria*) is a peptide preparation obtained by standardized enzymatic breakdown of purified brain proteins, and comprises 25% low-molecular weight peptides and free amino acids"* (pg. 272).

Table 6.9 The Effect of Cerebrolysin on Attention Post ABI

Author Year Country Research Design PEDro Sample Size	**Methods**	**Outcomes**
Alvarez et al. (2003) Spain Pre-Post N=20	**Population:** TBI; Mean Age=30.1 yr; Gender: Male=15, Female=5; Mean GCS=6.1; Time Post Injury Range=23-1107 d. **Intervention:** Patients with TBI received a total of 20 intravenous infusions of cerebrolysin solution (30 mL/infusion) over 4 wk. Assessments were made at baseline, during treatment, and after the 4 wk treatment period. **Outcome Measures:** Syndrome Kurztest (SKT), Electroencephalogram (EEG)/brain mapping recordings, Glasgow Outcome Scale (GOS).	1. Compared to baseline, patients with TBI showed a significant decrease in slow bioelectrical activity frequencies (delta: $p<0.010$; theta: $p<0.050$), and a significant increase in fast frequencies (beta: $p<0.010$) after receiving cerebrolysin, suggesting improvement in brain bioelectrical activity. 2. Significant improvements in SKT performance was noted from pre to post treatment (15.9±2.4 versus 12.0±2.1; $p<0.010$). 3. GOS scores significantly improved from pre to post treatment (3.7±0.3 versus 3.95±0.3; $p<0.050$).

Discussion

In an open-label trial of 20 patients with TBI Alvarez et al. (2003) found that cerebrolysin was associated with improved brain bioelectrical activity, as evidenced by a significant increase in fast beta frequencies. A brief neuropsychological battery (Syndrome Kurztest) consisting of nine subtests was administered to evaluate memory and attentional functions in patients undergoing treatment with cerebrolysin. There was an overall significant improvement in performance post treatment, suggesting patients experienced cognitive benefits from cerebrolysin treatment. Improvements in the Glasgow Outcome Scale were also observed (Alvarez et al., 2003). Together these findings suggest that cerebroylsin may represent an effective neuroprotective therapy with tangible cognitive benefits for individuals living with an ABI. However, controlled trials are necessary to further explore the efficacy of this drug.

Conclusions

There is level 4 evidence that cerebrolysin may improve attention scores post ABI.

Cerebrolysin may be beneficial for improving clinical outcomes and cognitive functioning following brain injury; however, controlled trials are needed to further evaluate its efficacy.

6.1.2.5 Rivastigmine

Rivastigmine is an acetylcholinesterase inhibitor which prevents the enzyme acetylcholinesterase from breaking down acetylcholine. This increases the concentration of acetylcholine in synapses. Acetylcholine has been most strongly linked with the hippocampus and memory impairments; however, it is also implicated in attentional processing.

Table 6.10 The Effect of Rivastigmine on Attention and Processing Speed Post ABI

Author Year **Country** **Research Design** **PEDro** ***Sample Size***	**Methods**	**Outcome**
Tenovuo et al. (2009) Finland RCT PEDro=10 N=102	**Population:** Mean age=45.5yr; Gender: Males=61, Female=39; Mean time post-injury=8yr; Mean GCS=11. **Intervention:** Individuals were randomized to receive one of two dosing rivastigmine schedules (placebo then rivastigmine or rivastigmine then placebo). Treatment lasted 8 weeks once a max dose of 12mg per day was reached. **Outcome Measures:** Computer-based reaction time (CRT), subtraction test, vigilance test (0-5mins, 5-10mins, 10-15mins, correct responses), Symptom Checklist-90 (SC), Diener satisfaction of life scale, Finnish Traumatic Brain Injury Questionnaire (FITBIQ).	1. The percentage of right answers in the subtraction tests were significantly different between groups (p<0.05), with the 2. Vigilance scores were significantly higher during periods of rivastigmine treatment compared to placebo treatments (p<0.05). 3. There were no other significant differences between groups on any other measures.
Silver et al. (2009) USA RCT PEDro=9 N=127	**Population:** TBI. *Ex-Rivastigmine* (n=65): Mean Age=36.9 yr; Gender: Male=43, Female=22; Time Post Injury=73.5 mo. *Ex-placebo* (n=62): Mean Age=38 yr; Gender: Male=42, Female=20; Time Post Injury=100.1 mo. **Intervention:** Participants were randomized to receive rivastigmine injections (1.5 mg 2x/d to a max of 12 mg/d) or placebo injection. **Outcome Measures:** Trails A and B, Hopkins verbal learning test (HVLT), Cambridge Neuropsychological Test Automated Batter Rapid Visual Information Processing (CANTAB RVIP A).	1. The mean final dose of rivastigmine was 7.9 mg/day. 2. 40% of patients were responders on CANTAB RVIP A' or HVLT score at week 38. 1. At the end of the study period all (n=98) were seen to improve of the CANTAB RVIP A' (p<0.001), the HVLT (P<0.001), and the Trails A and B (p<0.001). 2. Further sub-analysis controlling for order effects demonstrated no significant differences between groups.
Silver et al. (2006) USA RCT PEDro=9 N=123	**Population:** TBI. *Rivastigmine* (n=80): Mean Age=37 yr; Gender: Male=53, Female=27. *Placebo* (n=77): Mean Age=37.1 yr; Gender: Male=53, Female=24. **Intervention:** Participants were randomized to receive either rivastigmine (3-6 mg/d) or placebo.	3. Results of the CANTAB RVIP A' and HVLT found no significant differences between the placebo group and the treatment group. 4. Rivastigmine was found to be well tolerated and safe.

Author Year Country Research Design PEDro *Sample Size*	Methods	Outcome
	At the end of the first 4 wk, rivastigmine doses were increased to 3.0 mg, 2x/d. If necessary, doses were decreased to 1.5 mg or 4.5 mg 2x/d. **Outcome Measures:** Trails A and B, Hopkins verbal learning test (HVLT), Cambridge Neuropsychological Test Automated Batter Rapid Visual Information Processing (CANTAB RVIP A).	

Discussion

Three studies have concluded that rivastigmine most likely does not improve attention following an acquired brain injury (Silver et al., 2006; Silver et al., 2009; Tenovuo et al., 2009). In Silver's (2009) follow-up open-label cohort study to their original RCT (Silver et al., 2006), participants (n=98) showed significant improvement on the CANTAB RVIP A', the HVLT and the trail A and B scales at the end of 38 week study period; however, after further sub-analysis controlling for order effects no significant differences were found between groups. The third study by Tenovuo et al. (2009) found that rivastigmine significantly improved vigilance following doses of 12mg/day for eight weeks. Tenovuo et al. (2009) on average had higher doses and longer duration of rivastigmine administration compared to both Silver et al. studies; however, it is unclear whether this resulted in their conflicting results. The route of rivastigmine administration (injection versus oral administration) did not appear to influence its efficacy.

Conclusions

There is level 1b evidence that Rivastigmine compared to placebo is not effective for improving concentration or processing speed in post ABI individualsbut may increase vigilance.

Rivastigmine may not be effective in treating attention deficits post ABI.

6.1.2.6 Amantadine

Amantadine is a non-competitive N-methyl-D-aspartate receptor antagonist and has been used as an antiviral agent, prophylaxis for influenza A, treatment of neurological diseases such as Parkinson's Disease, and the treatment of neuroleptic side-effects such as dystonia, akinthesia and neuroleptic malignant syndrome (Schneider et al., 1999).

Table 6.11 Amantadine for the Treatment of Attentional Disorders Following an ABI.

Author Year Country Research Design PEDro *Sample Size*	Methods	Outcome
Hammond et al. (2018) United States RCT PEDro= 9 N=119	**Population:** Mean age=38.6yr; Mean time post-injury=6.2yr; Injury severity: GCS<13. **Intervention:** Individuals were allocated to receive either the placebo or 100mg amantadine twice a day for 60 days. Assessments were completed at baseline, day 28, and day 60. **Outcomes:** Digit-span from Wechsler Memory Scale-III (DS), Trail Making Test (TMT), Controlled Oral Word Association Test (COWAT), Learning/Memory Index (LMI), Attention/Processing Speed Index (APSI), overall composite (GCI).	1. No significant differences were seen on the DS, TMT, COWAT, or the APSI between groups at any time point. 2. The treatment group had significantly lower LMI scores at day 28 compared to the control group (p=0.001), this effect was not present at 60-day follow-up. 3. The treatment group had significantly lower scores on the GCI compared to the control group at day 28 (p=0.002), this effect was not present at day 60 follow-up.

Discussion

Presently, only one study has examined the effects of amantadine on attention and processing speed and found no significant effects on attention or processing speed following treatment. Any results which were found to be significant on other cognitive measures were not maintained at the 60-day follow-up (Hammond et al., 2018). Further studies are needed to examine whether or not amantadine may be a viable treatment for attention and processing speed deficits following an ABI.

Conclusions

There is level 1b evidence that amantadine is not effective for improving attention compared to placebo following an ABI.

Amantadine may not be effective in treating attention deficits following an ABI.

6.1.2.7 Hyperbaric oxygen therapy

Hyperbaric oxygen therapy involves the inhalation of pure oxygen under pressure allowing the lungs to absorb more oxygen per breath. Currently hyperbaric oxygen therapy is used to treat decompression sickness, serious infections, and delayed wound healing as a result of a comorbid illness such as diabetes (The Mayo Clinic, 2019).

Table 6.12 The Effect of Hyperbaric Oxygen Therapy on Attention and Processing Speed Post ABI.

Author Year Country Research Design PEDro *Sample Size*	Methods	Outcome
Hadanny et al. (2018) Israel Case Series N=154	**Population:** Mean age=42.7yr; Gender: Male=58.4%, Female=43.6%; Mean time post-injury=4.6yr; Injury severity: mild=44.8%, moderate=15.6%, severe=39.6%. **Intervention:** All individuals received hyperbaric oxygen therapy (HBOT). Sessions consisted of 60-90 mins of 100% oxygen at 1.5/2 ATA exposure 5 days a week. **Outcomes:** NeuroTrax software subsets: general, memory, executive functions, attention, information processing speed, visual spatial processing, motor skills.	1. On measures of general cognitive functioning there was a significant increase in scores after HBOT treatment ($p<0.0001$). 2. Memory scores significantly increased following HBOT treatment ($p<0.0001$). 3. Executive function scores significantly increased following HBOT treatment ($p<0.0001$). 4. Attentional scores significantly improved following HBOT treatment ($p<0.0001$). 5. Information processes speed significantly increased following HBOT treatment ($p<0.0001$). 6. Visual spatial processing significantly improved following HBOT treatment ($p=0.005$). 7. Motor skills significantly improved following HBOT treatment ($p<0.0001$).

Discussion

From this single case series, hyperbaric oxygen therapy significantly improved both attention and processing speed following treatment five days a week (Hadanny et al., 2018). Also, general improvements in cognitive functioning and visual processing were also reported (Hadanny et al., 2018). However, without proper prospective experimental data it is challenging to make conclusions on the efficacy of this intervention.

Conclusions

There is level 4 evidence that hyperbaric oxygen therapy may improve both attention and processing speed following an ABI.

Hyperbaric oxygen therapy may improve attention and processing speed following an ABI; however more prospective data is required in order to make a conclusion.

6.1.2.8 Dextroamphetamine

Dextroamphetamine is a central nervous stimulant; similar to methylphenidate, it is used to treat narcolepsy and attention deficit hyperactivity disorder. Dextroamphetamine is a noncatecholamine and sympathomimetic amine that acts as a stimulant, unfortunately more direct mechanisms of action are not currently known.

6.13 The Effect of Dextroamphetamine on Attention and Engagement Post ABI

Author Year Country Research Design PEDro *Sample Size*	Methods	Outcome
Hart et al. (2018) United States RCT PEDro=10 N=32	**Population:** *DEX Group (N=17)*: Mean age=39.6yr; Gender: Male=11, Female=6; Mean GCS=8.2; Mean time post-injury=53.6dy. *Control Group (N=15):* Mean age=38.7yr; Gender: Male=15, Female=0; Mean GCS=7.5; Mean time post-injury=60.2dy. **Intervention:** Participants either received the placebo or 10 mg of dextroamphetamine (DEX). Each treatment was administered once a day, in the morning, for 3 weeks. **Outcomes:** Moss Attention Rating Scale (MARS), Hopkins Rehabilitation Engagement Rating Scale (HRER), Cognitive Failures Questionnaire (CFQ), Rating Scale of Attentional Behavior (RSAB), Finger Taping Test (FT), the Symbol Digit Modalities Test (SDMT), Disability Rating Scale (DRS), Agitated Behavior Scale (ABS), Profile of Mood States (POMS),	1. There was a significant difference between groups on the ABS (p=0.04), with the DEX group demonstrating more agitation over time. 2. No other significant differences were found.

Discussion

Based on a single study, it does not appear that dextroamphetamine has any beneficial effects on attention or processing speed following an ABI. However, administration of dextroamphetamine did significantly increase agitation over time.

Conclusions

There is level 1b evidence that dextroamphetamine does not improve attention following an ABI.

Dextroamphetamine may not be an effective treatment for attentional deficits following an ABI and may actually increase agitation.

6.2 Rehabilitation of Learning and Memory Deficits

Memory impairment is one of the most common symptoms following brain injury and it is estimated that time and cost of care would be reduced if effective treatments were found to improve memory (Walker et al., 1991). When evaluating intervention strategies to improve memory performance following brain injury, the literature indicates that there are two main approaches to rehabilitation: restoration/retraining of memory, and compensation of deficits. Compensation includes "training strategies or techniques that aim to circumvent any difficulty that arises as a result of the memory impairment." (McLean et al., 1991). Compensatory techniques include internal aids, which are "mnemonic strategies that restructure information that is to be learned." (McLean et al., 1991). Conversely, interventions for remediation of memory deficits range from assistive technology to visual imagery. Cappa and colleagues (2005) reviewed various strategies used to improve memory deficits without the use of electronic devices, external aids were judged to be *"possibly effective.",* while specific learning strategies (e.g. errorless learning) were found to be “probably effective” depending upon the task used, the type of memory involved and the severity of the impairment. Several studies were identified examining interventions to improve learning and memory following ABI.

6.2.1 Non-Pharmacological Interventions

6.2.1.1 Assistive Devices

Assistive devices for aiding learning and memory can include anything from physical or external devices to internal memory strategies. The following section discusses a variety of aids that may be used to support individuals with memory or learning deficits as a result of an ABI.

6.2.1.1.1 External Technology Aids

External aids, of which there are active or high tech (computers, personal digital assistants (PDAs), and mobile phones) and passive or low technology/no technology (e.g., calendars, diaries, lists, timetables and dictaphones) devices, have been shown to assist with memory (McDonald et al., 2011). As active aids become more readily available, there is a greater need to study their effectiveness in helping those with an ABI deal with prospective memory impairments. Included here are studies which examined how external aids, both active and passive, could be used to enhance memory following brain injury.

Cicerone et al. (2000) recommended that the use of memory notebooks or other external aids “*may be considered for persons with moderate to severe memory impairments after TBI (and) should directly apply to functional activities, rather than as an attempt to improve memory function per se*.”

Table 6.14 The Effect of External Aids on Memory Post ABI

Author Year Country Research Design PEDro *Sample Size*	**Methods**	**Outcome**
Gracey et al. (2017) UK RCT PEDro=6 $N_{Initial}$=74, N_{Final}=59	**Population:** CVA=23, Infection=3, TBI=33, Tumor=10, Missing=1. *Control First (n=34)*: Mean Age=50.18 yr; Gender: Male=23, Female=11; Mean Time Post Injury=8.62 yr. *Assisted Intention Monitoring (AIM, n=36)*: Mean Age=46.36 yr; Gender: males=23, females=13; Mean Time Post Injury=4.89 yr. **Intervention:** Participants were randomized to receive AIM or control first. In the AIM-first group, participants received goal management training followed by text messages for improving achievement of everyday intentions. Control-first group received brain injury information, Tetris game, and non-informational text messages. After 3 wk, participants were crossed over with AIM-first group receiving usual care and control-first group receiving AIM. **Outcome Measures:** Mean daily proportion of intentions achieved, Achievement of all goals excluding the phone call task, Profile of Mood States total mood disturbance (POMS MD), Hotel Task, Verbal Fluency.	1. Participants achieved a greater proportion of intentions during the AIM intervention relative to control (p=0.040). 2. Participants achieved a greater proportion of goal attainment (without the phone call task) during the AIM intervention relative to control (p=0.033). 3. No significant Group x Time interaction effect was found for the POMS MD or Hotel Test. 4. When only comparing group differences at post-intervention phase 1, intention to treat analysis showed no significant difference between groups for proportion of intentions achieved or achievement of goals excluding the phone task.

Author Year Country Research Design PEDro *Sample Size*	Methods	Outcome
O'Neill et al. (2017) UK RCT PEDro=7 $N_{Initial}$=27, N_{Final}=24	**Population:** TBI=16, Subarachnoid hemorrhage=3, Other=5; Mean Age=45.14 yr; Gender: Male=22, Female=2; Mean Time Post Injury=5.53 yr; Severity: severe. **Intervention:** Participants were randomly assigned to the experimental (n=10) or control group (n=14), and assessed before (baseline), during, and after intervention (return to baseline). Experimental group participants received Guide, an audio-verbal interactive micro-prompting software designed to emulate the verbal prompts and questions provided by carers or support workers. Control group participants received rehabilitation as usual. **Outcome Measures:** Morning Checklist (number of support worker prompts, number of safety critical and general errors, deviations from and repetitions of the necessary sequence), Satisfaction score (5-point scale).	1. Compared to baseline, there was a significantly greater reduction in the intervention group than the control group during (p<0.010) and after (p<0.010) the intervention for the number of prompts needed. 2. There were no significant differences between groups across the three phases in terms of number of errors, sequence errors, or satisfaction scores.
Lannin et al. (2014) Australia RCT PEDro=8 N=42	**Population:** TBI; Mean Age=33.5 yr; Gender: Male=26, Female=16; Mean Time Post Injury=9.2 yr. **Intervention:** Participants were randomly allocated to either the experimental group (EG; n=21), who received 8 weeks of training in the use of a personal digital assistant (PDA) with an occupational therapist, or the control group (CG; n=21) who received 8 weeks of traditional occupational therapy. Training sessions for the EG focused on PDA training for application and organization into everyday life. **Outcome Measures:** Goal Attainment Scale (GAS), Memory Functioning Questionnaire (MFQ) and Memory Compensation Questionnaire (MCQ).	1. There was a significant difference between EG and CG groups in the functional memory failures subset of the GAS (p=0.0001); however, the total GAS score was not significant between groups (p=0.165). 2. The caregiver report on the frequency of forgetting and retrospective memory subset of the MFQ were significant between groups (p=0.021, p=0.042 respectively); however, seriousness of forgetting and mnemonic usage subset of the MFQ were not significant between groups (p=0.455, p=0.301 respectively) 3. Internal strategies subset of the MCQ was significant between groups (p=0.021); however, external strategies subset of the MCQ was not significant between groups (p=0.580).
De Joode et al. (2013) Netherlands RCT PEDro=5 N=34	**Population:** TBI=11; Stroke=12; Mixed stroke/TBI=3; Other=8; Gender: Male=24, Female=10. *Experimental Group (n=21):* Mean Age=42.2yr; Mean Time Post Injury=38.9mo. *Control Group (n=13):* Mean Age=39.4yr; Mean Time Post Injury=65.9mo. **Intervention:** Participants were randomized to either: 1) Control Group: care as usual (paper and pencil aids) aimed at learning skills to support memory, planning and organization, or 2) Experimental Group: participants were trained to use Personal Digital Assistants (PDAs) as a cognitive aid to compensate for dysfunctions. After 8hr of training (T1), 16hr of training (T2), and at 5mo follow-up (T3), assessments were conducted. **Outcome Measures:** Goal Attainment Scaling (GAS), Cognitive Failure Questionnaire, Frenchay	1. GAS improved significantly from baseline to T2 for both groups. The experimental group showed a mean increase of 45.2 (p<0.001) and the control a mean increase of 36.7 points (p<0.001); however, the between-group analysis was not significant (p>0.05). 2. None of the other outcome measures differed significantly between groups at T1 or T2 (p>0.05).

Author Year Country Research Design PEDro *Sample Size*	Methods	Outcome
	Activities Index, General perceived Self-Efficacy Scale, Utrecht Coping List.	
Powell et al. (2012) USA RCT PEDro=7 N=29	**Population:** TBI=23, ABI=6; Mean Age=42.31 yr; Gender: Male=17, Female=12; Mean Time Post Injury=13.59 yr. **Intervention:** Patients were assigned to either the systematic instruction group (n=15) or the conventional group (control; n=14). The systematic group was based on direct instruction and mastery, rather than exploratory learning (e.g., errorless learning). The control group received conventional, trial and error learning (e.g., errorful learning). Participant's sessions targeted selected skills on a personal digital assistant (PDA; Palm Tungsten E2). All participants received 12 sessions (45 min, 2-3 x/wk for 4-6 wk). **Outcome Measures:** Assessment of PDA skills, California Verbal Learning Test II-Short Form, Wechsler Memory Scale III (Logical Memory, Visual Reproduction), Controlled word Association Test, Trail Making A and B.	1. Those receiving systematic instruction performed significantly more (p<0.01) correct tasks at the 30-d follow-up compared to participants receiving the conventional instruction. 2. Those receiving systematic instruction also performed the correct tasks more quickly (16 sec) than the conventional instruction group (41.15 vs 57.73 sec, p=0.050). 3. Fluency scores (ability to follow through with a task) were also found to be higher in those in systematic instruction group compared to those in the conventional instruction group at 30 d follow-up (p=0.050). 4. There was no statistically significant main effect on treatment condition for content generalization. 5. Overall systematic instruction resulted in better environmental generalization compared to trial and error learning (p<0.050) at post-test, but not 30d follow-up.
Dowds et al. (2011) USA RCT PEDro=5 N=36	**Population:** TBI patients: Mean age: 42.1 yr (Age Range: 16-66 yr); Gender: male=17, female=19; **Intervention:** Participants were trained on how to use two Personal Digital Assisant devices (Palm OS and Microsoft OS device) to assist them in organizing activities that needed to be completed throughout the week. Participants were randomly assigned to four memory aid conditions (Palm OS, Microsoft OS, Combined Baseline, or paper organizer) in a crossover fashion. **Outcome Measure:** Timely completion rates.	1. When using the PDAs, the individuals had a higher task completion rate than when they used paper memory aids (Palm OS: p<0.005; Microsoft OS: p<0.001). 2. Results also indicated that those using the Palm OS PDA had a higher completion rate than those using the Microsoft OS PDA (p<0.0005).
Lemoncello et al. (2011) USA RCT PEDro=5 N=23	**Population:** Group A (n=12): Mean age=47.17 yr, mean time post-injury=9 yr; Group B (n=11): Mean age=47.55 yr, Mean time post-injury=12.45 yr. **Intervention:** Patients were randomly assigned to group A or group B. In group A participants were assigned to use the Television Assisted Prompting (TAP) system, which gave them personalized task reminders through their television, in the crossover phase participants used their own typical practice (TYP) strategies of remembering what tasks they had to complete. In group B participants started with the TYP phase, and then at crossover used the TAP system. **Outcome Measures:** Task completion.	1. No significant differences were found between groups A or B; therefore, data from the two groups was collapsed. 2. Task completion was significantly better when participants used the TAP condition (72%) versus the TYP condition (43%). 3. In the TAP condition participants completed significantly more experimental tasks compared to either preferred (p=0.01) or non-preferred tasks (p=0.01).
Hart et al. (2002) USA RCT PEDro=5	**Population:** TBI: Mean Age: 31.5 yr; Gender: male=8, female=2. **Intervention:** Individualised current therapy goals were randomly assigned to a portable voice	1. Recorded goals were recalled significantly better than unrecorded goals (p<0.010).

Author Year Country Research Design PEDro *Sample Size*	Methods	Outcome
N=10	organizer (n=3) or not having an organizer (n=3), 2-5 days per week. **Outcome Measure:** Recall of goals.	
Wilson et al. (2001) UK RCT PEDro=4 N=143	**Population:** Mean Age: 38.57 yr; Gender: Male=105, female=38; Mean Time Post-Injury: 4.9 yr; Condition: TBI=63 (44.1%), Stroke=36 (25.2%), Other: ABI=44 (30.7%). **Intervention:** After a 2-week baseline, patients were randomized into two groups: Group A received a pager first and Group B was put on a waiting list. After 7 weeks of treatment patients switched conditions. Measures were taken during the last 2 weeks of each treatment period/ Patients chose their own tasks in which they wanted to be reminded. **Outcome Measures:** Patients' Ability to Successfully Carry out Everyday Tasks.	2. During the last 2 weeks of the 7-week treatment period, the participants using the pager were significantly more successful in achieving target behaviors than the waiting list group (p<0.001).
Evald (2018) Denmark Pre-Post N=13	**Population:** Mean age=41.5yr; Gender: Male=11, Female=2; Injury severity: mean GCS=6.6; Mean time post injury=11 yrs. **Intervention:** Each individual received a Windows Phone (version 7.5) for 6-weeks and was asked to use this as their only memory strategy. Five group sessions (1.5 hrs each) were held to help ensure each individual knew how to use the applications on each phone (calendar, reminders, etc.). After the 6-week intervention period a 2-week break was taken to assess all behaviors and then a 6-week follow-up assessment was completed. **Outcome Measures:** Prospective Memory Questionnaire (PMQ), Prospective and Retrospective Memory Questionnaire, Cognitive Failures Questionnaire (CFQ), European Brain Injury Questionnaire (BIQ), Hospital Anxiety and Depression Scale (HADS).	1. Pre- to post-intervention the PMQ (p=0.005) and the Prospective and Retrospective Memory Questionnaire (p=0.014) revealed a significant decrease in the number of self-reported memory problems. 2. No significant effects were found on common brain injury deficits through the BIQ and CFQ. 3. No significant effects on mood were reported through the HADS or QoL scale. 4. When comparing reports from baseline to 6-week follow-up, significant effects on memory and self-reported errors were seen on PMQ (p=0.009), the Prospective and Retrospective Memory Questionnaire (p=0.014), and the CFQ (p=0.000).
Evald et al. (2015) Denmark Pre-Post N=13	**Population:** TBI; Mean Age=41.5 yr; Gender: Male=11, Female=2; Mean Time Post Injury=11 yr; Mean GCS=6.6. **Intervention:** Participants underwent memory training using smartphones (1 individual and 5 group sessions, 1.5 hr/session, 1 session/wk, for 6 weeks). In the individual session participants were instructed on smartphone setup. During the group sessions participants were instructed on compensatory memory strategies using appointment, tasks and contacts applications. Each group session was completed in 4 steps; 1) introduction to the memory strategy, 2) demonstration of the application, 3) exercises with examples and 4) homework instructions. **Outcome Measure:** Self-reported measures of overview, memory, stress and fatigue.	1. 5 of the 13 participants reported memory improvements following smartphone use, while the remaining reported no change. 2. 3 of the 13 participants reported stress improvements following smartphone use while the remaining reported no change. 3. 1 of the 13 participants reported fatigue improvements following smartphone use while the remaining reported no change. 4. 9 of the 13 participants reported a positive overview of smartphone use while the remaining reported no change. 5. There were no negative events reported.

Author Year Country Research Design PEDro *Sample Size*	Methods	Outcome
Waldron et al. (2012) Ireland Pre-Post N=5	**Population:** TBI=3, CVA=1, Tumour=1; Mean Age=48.8yr; Gender: Male=4, Female=1; Mean Time Post Injury=23.2yr. **Intervention:** Participants were given personal digital assistants (PDAs) and a series of seven prospective memory (PM) tasks that they needed to complete. Baseline measures were taken for three weeks, followed by two weeks of PDA condition. More specifically, the PDA was a palmtop computer (Palm IIIe). **Outcome Measure:** Completed tasks.	1. Compared to baseline when internal memory only was used, the use of the PDA significantly improved PM task completion from 59.04% to 90.00% completion (p<0.05).
Gentry et al. (2008) Canada Pre-Post N=23	**Population:** TBI patients: Age Range 18-66 yr; Gender: Male=16, Female=7; Time Post-Injury=1-34 yr. **Intervention:** Participants were each given a PDA and trained on how to use it by an occupational therapist (OT). **Outcome Measure:** Craig Handicap Assessment and Rating Technique Revised (CHART); Canadian Occupational Performance Measure (COPM).	2. On the COPM, improvements were noted when looking at post training performance and post training satisfaction (p<0.001). 3. Scores on the CHART-R self-assessment rating scale showed improvement as well post-training (p<0.001). 4. Significant improvement was seen on the scores of the cognitive independence, mobility, and occupation subsections of the test (p<0.001).
Fish et al. (2007) UK Case Series N=20	**Population:** Age Range: 19-60 yr; Gender: Male=15, Female=5; Condition: TBI=14, Other=6. **Intervention:** Participants were trained to associate the text message 'STOP" with a cue for participants to stop and think about what needed to be done, what they were doing etc. Participants were asked to make telephone calls at specific times of the day for a 3-week period. Over the 3-week period on 5 randomly selected days a text message "STOP" was sent to participants. **Outcome Measure:** Completion of task.	1. During the first week 15% of the participants failed to make the calls. 2. The effect of cueing on participants had a significant impact on the number of calls made (p<0.001). 3. Participants made 87.6% of calls when cued but only 71.2% of calls when they were not cued. 4. Of note there was a positive relationship between the number of calls made (completed) and the time in which they were made (within 5 minutes of the target time).
Burke et al. (2001) USA Pre-Post N=5	**Population:** Mean Age: 50 yr; Condition: TBI=3, SAH=2. **Intervention:** Assessing patient's ability to use a patient locator and minder (PLAM) system to assist in their adherence to therapy schedules. Patients were prompted by hospital staff about appointment times when necessary. **Outcome Measure:** Number of human prompts necessary to direct a patient to a therapy destination.	1. Average number of human prompts declined significantly using the PLAM system by more than 50% (p<0.001) and the number of sessions requiring no prompting increased from 7 to 44% (p<0.005). 2. Patients arrived on average 1.3 minutes earlier using PLAM – a 6.1-minute improvement over baseline.
Wright et al. (2001a) UK Pre-Post N=12	**Population:** Mean Age: 39 yr; Gender: male=10, female=2; Mean Time Post-Injury 3yr; Condition: TBI=9, Subarachnoid Hemorrhage=2. **Intervention:** Two different computer aid formats for 2 months (with a one-month gap between machines). **Outcome Measure:** Attitudes, Usage, Relation to Psychometric Factors.	1. Appointment diary was used more than any other aid. 2. High users made more new diary entries (p<0.060) suggesting a conceptual understanding of how to use memory aids in everyday living was a prerequisite for benefiting from them.

Author Year Country Research Design PEDro *Sample Size*	Methods	Outcome
Wright et al. (2001b) UK Pre-Post N=12	**Population:** Mean Age: 34 yr; Gender: male=6, female=6; Mean Time Post-Injury=6 yr. **Intervention:** Two-month comparative study of Casio and HP electronic organizers (one-month break between brands). **Outcome Measure:** Frequency of use.	1. No significant correlations between any single psychometric measure and organizer entries. 2. People accustomed to using memory aids (any type) made more use of pocket computers (p<0.070). 3. Low frequency users were put off organizers when it had a physical keyboard (p<0.010). 4. High frequency users used the keyboard more (p<0.070).
Kim et al. (2000) USA Case Series N=12	**Population:** Age Range: 22-67 yr; Gender: male=8, female=4; Condition: TBI=11, CVA=1; **Intervention:** Supervised usage trial of a palmtop computer that included scheduling software capable of generating audible reminder cues. **Outcome Measure:** Survey of subjects' use of computer as an aid.	1. Nine subjects (75%) reported that the palmtop computer had been a useful tool. 2. Seven of these 9 patients expressed that they continued to use the computer following the completion of the study. 3. All patients recommended that the computer continue to be used in outpatient brain injury rehabilitation.
van den Broek et al. (2000) UK Case Series N=5	**Population:** Age Range: 25-56 yr; Gender: male=4, female=1; Time Post Injury: 19-54 mo; Condition: TBI=1, ABI=4. **Intervention:** Evaluate the effectiveness of the external aid "the Voice Organizer" for a period of 3-weeks. Messages could be dictated into the organizer and verbal reminders were repeated at specified times throughout the day. **Outcome Measure:** Positive and Negative Affect Schedule (PANAS)	1. All patients benefited from the introduction of the Voice Organizer as measured using the message-passing task and the Positive and Negative Affect Schedule (PANAS).
Wilson et al. (1997) UK Pre-Post N=15	**Population:** Gender: male=11, female=4; Condition: TBI=10, Stroke=1; ABI=4. **Intervention:** Evaluation of a Neuropage, a portable paging system. Patients assessed at baseline and after treatment. **Outcome Measure:** Task completion.	1. There was a significant improvement in task completion between the baseline and treatment phase of each subject (p<0.050). 2. Mean success at baseline was 37.08%, during treatment (85.56%) and post-treatment (74.46%).

PEDro = Physiotherapy Evidence Database rating scale score (Moseley et al., 2002a).

Discussion

Many studies have been conducted examining the effectiveness of various active reminders used for those with memory impairment. With advances in technology, more sophisticated organizers integrating these tools into personal digital assistants (PDAs) and smartphones have been studied. Patients accustomed to using memory aids were more likely to make use of computerized organizers (Wright et al., 2001b). Dowds et al. (2011) found that two different PDAs improved task completion rates compared to a paper-based schedule book, while Lannin et al. (2014) found that the use of a PDA in addition to conventional occupational therapy significantly reduced memory failures and forgetting. Multiple other studies have also found positive effects for the use of PDAs on memory (De Joode et al., 2013; Gentry et al., 2008; Powell et al., 2012; Waldron et al., 2012). However, the variety of available electronic organizers and learning curve for use prevent clear conclusions across studies. An RCT by Powell et al. (2012) demonstrated the importance of systematic instruction, as they compared direct instructions to conventional, trial and error patient learning on a PDA. Those receiving systematic instruction were superior in the number and speed of correct PDA tasks compared to conventional trial and error learning group. No differences were found between groups based on PDA input (physical vs touch-screen keyboard), provided the three core memory aid components of appointment diary, notebook, and to-do list were maintained (Wright et al., 2001a).

Smartphones represent a relatively new area of accessible technology and provide the user with many benefits. Smartphones are already designed to send notifications about their use, as well as multiple companies design apps for each phone brand interface allowing individuals to keep their current devices and still access helpful applications. The most common advantages to smartphones are reminders/alarms and ability to combine a calendar, tasks list, contacts, mail, and phone on one device. Disadvantages include the loss of battery life and risk of dependency on the assistive device; however, these are minor inconveniences in comparison to the reported improvement in memory in some patients (Evald, 2015). The increasing availability of smartphones also creates the ability to enhance current therapies with text messages. A case series by Fish et al. (2007) demonstrated that participants could be trained to associate a text message with stopping and thinking about what needed to be done, with participants more likely to remember the instruction to call the investigators when texted the message "STOP". On measures such as the Prospective and Retrospective Memory Questionnaire, the use of smartphones was shown to significantly reduce the number of self-reported errors (Evald, 2018). Gracey et al. (2017) also found that goal management training could be supplemented with text messages for improving achievement of everyday intentions, with individuals who received text prompt more likely to succeed in their goals compared to those not receiving prompts. This effect was not observable once the texts had stopped to both groups.

Wilson et al. (1997) found that a portable paging system, NeuroPage, could reduce everyday memory problems and improve task completion. A crossover RCT also demonstrated that the pager system significantly increased participants' ability to carry out daily tasks, and successful task achievement was more efficient after the pager intervention was introduced (Wilson et al., 2005; Wilson et al., 2001). However, the need for a centralized system to send reminders reduces the feasibility of pagers since many people may be able to achieve the same results using other electronic reminder systems.

Voice organizers have also been shown to improve goal execution. In a study by Kim et al. (2000), 12 TBI patients were given palmtop computers programmed with scheduling software capable of generating audible reminder cues. Patient feedback suggested that the use of the palmtop computer was beneficial for their rehabilitation, and over half of the patients continued to use the device even after the conclusion of the study. In addition, one case series (van den Broek et al., 2000) and one RCT (Hart et al., 2002) found that voice organizers helped to improve recall of previously identified goals.

External memory aids can also be incorporated into an individual's home or work environment. Lemoncello et al. (2011) developed a television assisted prompting (TAP) system that provided reminders of events to be completed through the television screen. This crossover RCT found that compared to traditional methods (paper planner, cell phones or computers), participants using the TAP system completed significantly more tasks (Lemoncello et al., 2011).

These external aids can also be adapted for use in an in-patient setting. O'Neill et al. (2017) developed an audio-verbal interactive micro-prompting system, Guide, designed to emulate the verbal prompts and questions provided by caregivers or support workers. The number of support workers prompts needed during their morning routine was reduced, even though there were no significant differences between groups in terms of the number of errors and satisfaction scores (O'Neill et al., 2017). An acute rehabilitation unit also showed efficacy for a computerized tracking system designed to locate patients and send reminders when patients moved in the wrong direction for appointments (Burke et al., 2001). By reducing the number of staff prompts needed, these systems can increase patient independence and help free-up support personnel for other tasks.

Conclusions

There is level 4 evidence that the NeuroPage system may increase a patient's ability and efficiency to complete tasks post TBI.

There is level 2 evidence that voice organizer programs are effective at improving recall of goals and are found to be effective by post TBI patients.

There is level 1b evidence that the use of a personal digital assistant (PDA) in combination with conventional occupational therapy is superior to occupational therapy alone at improving memory in patients post TBI.

There is level 2 evidence that personal digital assistants (PDAs) are superior to a paper-based schedule book at improving task completion rates post TBI.

There is level 1b evidence that use of a personal digital assistant (PDA) after receiving systematic instructions is superior to PDA trial and error learning at improving the number and speed of correct tasks post TBI.

There is level 1b evidence that reminder text messages sent to patients through their smartphones, whether alone or in combination with goal management training, improves goal completion post TBI.

There is level 2 evidence that a television assisted prompting (TAP) system is superior to traditional methods of memory prompting (paper planners, cell phones, computers) at improving the amount of completed tasks post TBI.

There is level 1b evidence that the audio-verbal interactive micro-prompting system, Guide, can reduce the amount of support-staff prompts needed for the patient to complete a task post TBI.

There is level 4 evidence that a computerized tracking system that sends reminders to patients when they are moving in the wrong direction reduces the amount of support-staff prompts needed for patients to complete a task post TBI.

Pager and voice-organizer programs may improve a patient's ability to complete tasks post TBI.

Personal digital assistant (PDA) devices are superior to paper-based interventions at improving memory and task completion post TBI; specially when introduced using systematic instructions and in combination with occupational therapy. Patients who have used previous memory aids might benefit from this intervention the most.

Text message prompts sent to a patient's smartphone, when used alone or in combination with other memory-improvement therapies, likely improve task completion post TBI. However, risk

exists of device dependency exists.

A television assisted prompting (TAP) program may be superior to other methods of memory prompting in post TBI patients.

Automated prompting systems, such as Guide (audio-verbal interactive micro-prompting system) and a computerized tracking system, can reduce the number of prompts needed from support staff to patients to complete tasks post TBI.

6.2.1.1.1.1 External Passive Techology or Non-Technology Aids

Passive devices are those that do not require specific electronic programming for their use such as paper calendars, notebooks, and planners. A variety of studies have examined the effects of these standard tools on learning and memory; however, the amount of studies has been quickly outpaced by studies examining technology as it becomes more readily available.

Table 6.15 The Effect of Passive Devices on Memory and Task Completion Post ABI

Author Year **Country** **Research Design** **PEDro** ***Sample Size***	**Methods**	**Outcome**
McDonald et al. (2011) UK RCT PEDro=5 N=12	**Population:** Mean Age: 47yr; Gender: male=6, female=6; Condition: TBI=4, Stroke=4, Other ABI=3. **Intervention:** One of two groups (Group A or Group B). All were asked to complete weekly monitoring forms indicating what activities they would like to complete within the next 15 weeks. Those assigned to Group A (the Google calendar group) were shown how to use the calendar to remind them of upcoming activities. They were discouraged from using other reminder strategies during the next 5 weeks. Group B was the standard diary group. At the end of the 5 weeks, group B began using the Google calendar while Group A began using the standard diary. **Outcome Measure:** Task completion.	1. Overall the use of memory aids assisted individuals in completing tasks as opposed to no memory aids. 2. Memory performance was greater using the google calendar compared to the standard diary (p<0.001). 3. During the Google Calendar intervention phase, there was 40.6% increase in completing their prospective intention compared to the standard diary phase. 4. Overall 82% of targets were reached using Google calendar but only 55% using the standard diary.
Bergquist et al. (2009) USA RCT N=14	**Population:** TBI; Mean Age=48yr; Gender: Male=7, Female=7. **Intervention:** Patients were allocated to either an active calendar acquisition intervention group or the control diary intervention group. Throughout each intervention, participants had 30 therapist-mediated sessions, which were completed via Instant Messaging (IM). At the end of the 30 sessions they crossed-over to the other group. During the calendar condition, participants were encouraged to use the online calendar to plan and remember events. IM sessions were used to review tasks completed.	1. There were no significant differences between the Calendar and the Diary conditions on patient- and family-rated mood and memory functioning as noted on the NFI; there were no differences on CIQ total score as well. 2. From baseline to the last follow-up, improvement was found on the CTQ, specifically in the notes on calendar (p<0.02) and the use of cue cards (p<0.01). Family members also noted improvement in levels of depression (p<0.02) and reported fewer memory problems p<0.004).

	Outcome Measure: Neurobehavioural Functioning Inventory (NFI), Community Integration Questionnaire (CIQ), Compensation Techniques Questionnaire (CTQ).	
Ownsworth & McFarland (1999) Australia RCT PEDro=3 N=20	**Population:** Mean Age: 43.1 yr; Gender: male=19, female=1; Condition: TBI=15, Stroke=1, Other ABI=4; Injury etiology: traffic accident (n=12), sport injury (n=1), assault (n=2), tumour (n=2), stroke (n=1), and infection (n=2). **Intervention:** Randomized into a diary only (DS) group (n=10) and a diary & self-instructional training (DSIT) group (n=10) intervention. The DS group participated in a 6 week "Bottom-Up" approach program that emphasized the development of functional skills using compensation based, on task,-specific learning. The DSIT group participated in a 10 week "Top-Down" approach program that emphasized the capacity for self-regulation and self-awareness using "Self Instructional Training." **Outcome Measure:** Self report questionnaire on commonly experienced memory problems.	1. All subjects reported significantly fewer problems with memory ($p<0.001$) and lower levels of distress ($p<0.01$) during treatment phase when compared to baseline. 2. There was a significant increase in the degree of strategy use during treatment ($p<0.05$) regardless of type of diary training. 3. There were no significant differences between the DS and DSIT groups ($p>0.05$).
Watanabe et al. (1998) USA RCT PEDro=3 N=30	**Population:** Mean Age: 53.4yr; Gender: male=24, female=6; Condition: TBI=16, ABI=14. **Intervention:** Patients were randomized into two groups, one group had in-room calendars (n=14) and the other did not (n=16). The Temporal Orientation Test was given daily, when errors were made, corrections were shown on the in-room calendars (for the experimental group). **Outcome Measure:** Temporal Orientation Test (TOT).	1. Presence of a calendar did not significantly affect TOT scores.
Schmitter-Edgecombe et al. (1995) United States RCT PEDro=8 N=12	**Population:** *Notebook Training (N=4):* Mean age=29.9yr; Mean time post-injury=77.7mo. *Supportive Therapy (N=8)*: Mean age=26.8yr; Mean time post-injury=86.8mo. **Intervention:** Individuals were randomly assigned to either a memory notebook use group, or a supportive therapy group (control) for 9 weeks. Individuals were assessed at baseline, immediately following treatment, and at 6-months follow-up. **Outcome Measures:** Everyday memory failures (EMFs), laboratory-based memory (Rivermead Behavioral Memory Test), laboratory-based recall (Logical Memory I and II, Visual Reproduction I and II from Wechsler Memory Scale), Everyday Memory Questionnaire (EMQ).	1. Participants did not differ significantly on any baseline measures. 2. There were no significant differences groups on laboratory-based recall, laboratory-based everyday memory, or EMQ scores. 3. Participants in the notebook group experienced significantly fewer EMFs compared to the supportive therapy group ($p<0.05$). However, this effect was no longer significant at follow-up.

PEDro = Physiotherapy Evidence Database rating scale score (Moseley et al., 2002a).

Discussion

Multiple RCTs have examined the use of calendars and calendar tools on learning and memory (Bergquist et al., 2009; McDonald et al., 2011; Ownsworth & McFarland, 1999; Schmitter-Edgecombe et al., 1995; Watanabe et al., 1998). In one RCT by McDonald et al. (2011), the use of a Google calendar was compared to the use of diary tracking. It was found that although both groups achieved a fair number of desired tasks, those using the Google calendar had a significant increase in task completion through the use of automated reminders and messages. A second RCT also compared the use of a calendar to diary use (Bergquist et al., 2009). However, in this instance no significant between-group differences were found with both reporting positive results on memory. In another RCT (Ownsworth & McFarland, 1999), diary use was examined alone as well as with the combination of self-instructional training. On self-reported memory scales, all subjects reported improvements in memory, as well as significant increases in the degree of memory strategies used regardless of diary training. There were no significant differences between groups on memory performance however (Ownsworth & McFarland, 1999). Comparing the use of a memory tool (notebook) to generalized supportive therapy, the use of a notebook specifically was shown to result in a greater reduction in memory failures (Schmitter-Edgecombe et al., 1995); however, this effect was lost at 6-month follow-up. Lastly, Watanabe et al. (1998), found no significant effects of calendar use on a test of orientation, compared to no calendar use when individuals were still inpatients.

Conclusions

There is level 2 evidence the use of an electronic calendar is superior to the use of a diary for improving memory in individuals with an ABI.

There is level 2 evidence that the presence of a diary with or without self-instructional training improves memory following an ABI.

There is level 2 evidence that the presence of a calendar may not improve orientation post ABI.

There is level 2 evidence that diary training in combination with self-instructional training may be more effective than diary training alone at improving memory and task completion post ABI.

Calendars may be effective tools for improving memory and task completion post ABI.

The use of a diary may help to improve memory and task completion post ABI.

6.2.1.1.1.2 Virtual Reality

Virtual reality (VR) allows individuals to interact with and experience a virtual environment in three-dimensions, realistically simulating different situations/environments/tasks through immersive (head-mounted display) or non-immersive (computer monitor or projector screen) multimedia (Sisto et al., 2002). VR systems are constantly evolving, providing a safe and motivating environment for practicing real life scenarios (Shin & Kim, 2015). A systematic review by Shin and Kim (2015) found that VR may be an effective cognitive therapy, though the limited low quality evidence has prevented strong conclusions. On observational study by Canty et al. (2014) demonstrated that VR might also be potentially helpful as an assessment tool. Individuals with a brain injury performed more poorly on a series of VR tasks compared to healthy controls (Canty et al., 2014).

Table 6.16 The Effect of Virtual Reality Exercises on Learning and Memory Post ABI

Author Year Country Research Design PEDro Sample Size	Methods	Outcome
Yip & Man (2013) Hong Kong RCT PEDro=5 N=37	**Population:** ABI. *Treatment Group (TG, n=19):* Mean Age=37.83yr; Gender: Male=12, Female=7; Mean Time Post Injury=145.13d. *Control Group (CG, n=18):* Mean Age=38.53yr; Gender: Male=12, Female=6; Mean Time Post Injury=167.53d. **Intervention:** Participants were randomized to receive virtual-reality (VR) prospective memory (PM) training (TG) or control (CG). VRPM training consisted of event-based tasks, time-based tasks, ongoing tasks, and recall tasks in both visual and auditory formats. Control training consisted of reading and games. Both were received in 30min sessions 2/wk for a total of 6wk. Outcomes were assessed at baseline and after treatment. **Outcome Measures:** VR-based PM test (VRPMT); Real life behavioural PM test (RLPMT); Cambridge Prospective Memory Test–Chinese Version (CAMPROMPT-CV); Hong Kong List Learning Test (HKLLT); Frontal Assessment Battery (FAB); Word Fluency Test–Chinese Version (WFT-CV); Colour Trails Test (CTT); Community Integration Questionnaire–Chinese Version (CIQ-CV); Self-efficacy questionnaire (SEQ).	1. In the TG, VRPMT showed significant improvements after treatment on immediate recall of tasks (p<0.05), number of time checks (p<0.001), and performance of event-based (p<0.001), time-based (p<0.001), and ongoing (p<0.01) tasks compared to baseline. No significant difference was found on delayed recall of tasks or total time lapsed. 2. In the TG, RLPMT showed significant improvements after treatment in event-based (p<0.01) and time-based (p<0.01) tasks, but not ongoing tasks, compared to baseline. 3. In the TG, significant improvements were found after treatment on CAMPROMPT-CV (p<0.05), FAB (p<0.01), WFT-CV (p<0.01), and SEQ (p<0.01) compared to baseline. No significant difference was found on HKLLT, CTT, or CIQ-CV. 4. In the CG, no significant difference was found after treatment on any outcome measure compared to baseline. 5. After treatment, a significant difference was found between groups on event-based tasks of RLPMT (p<0.05), FAB (p<0.01), WFT-CV (p<0.05), and CTT (p<0.05). No significant difference was found between groups on VRPMT, CAMPROMPT-CV, HKLLT, CIQ-CV, or SEQ.
Grealy et al. (1999) Scotland RCT PEDro=1 N=13	**Population:** TBI patients: Age Range: 19-64; Gender: male=8, female=5. **Intervention:** Crossover design: patients were allocated to a 4-week intervention of receiving Virtual reality (VR) exercise or a no-exercise control condition. **Outcome Measure:** Tests measuring attention, information processing, learning, memory, and reaction and movement times.	1. Intervention group (n=13) performed significantly better than control group (n=320) on digit symbol (p<0.01), verbal (p>0.01) and visual (p<0.05) learning tasks. 2. Reaction (p<0.01) and movement (p<0.05) times improved significantly after a single VR session.
Dahdah et al. (2017) USA Pre-Post $N_{Initial}$=21 N_{Final}=15	**Population:** CVA=6, TBI=5, Tumor=2, Anoxia brain injury=2; Mean Age=40.3yr; Gender: Male=12, Female=3. **Treatment:** Participants received the virtual reality (VR) intervention sessions (apartment and classroom) twice per week for a 4wk period. Sessions 1 and 8 included all types of distractors, sessions 2 and 3	1. No statistically significant performance differences were found from baseline to conclusion of the study for the VR apartment Stroop or D-KEFS Stroop test. 2. For the VR classroom, participants' shortest response time on the word-reading condition was significantly

	included no distracting stimuli, sessions 4 and 5 included only auditory distracting stimuli, and sessions 6 and 7 included only visual distracting stimuli. **Outcome Measure:** Woodcock-Johnson, 3rd edition (WJ-III pair cancellation subtest), Delis-Kaplan Executive Function System (D-KEFS Color-Word Interference subtest), Automated Neuropsychological Assessment Metrics (ANAM Go/No-Go and unimodal Stroop subtests), VR Stroop task (apartment and classroom).	reduced by session 8 (p=0.0383). All other VR classroom Stroop variables did not show significant differences. 3. No significant differences from session 1 to session 8 were found for all pair cancellation subtest scores. 4. From session 1 to 8, the ANAM Stroop word-reading percentage of items with a correct response (p=0.0293), ANAM Stroop word-reading number of correct responses per minute (p=0.0321), and ANAM Go/No-Go number of impulsive/bad responses (p=0.0408) significantly increased. All other ANAM variables did not show significant differences.
Sorita et al. 2013 France PCT N=27	**Population:** TBI. *Treatment Group (TG, n=14):* Mean Age=31.1; Gender: Male=12, Female=2; Mean Time Post Injury=4.67yr; Mean GCS=5.8. *Control Group (CG, n=13)*: Mean Age=31.1; Gender: Male=13, Female=0; Mean Time Post Injury=6.77yr; Mean GCS=6.7. **Treatment:** Participants engaged in the same route-learning task in either a real urban environment (CG) or a virtual simulation of that environment (TG). After a learning phase, participants repeated the task twice in a row and >24h later. Outcomes were assessed after each repetition and a series of tests was completed after the last repetition. **Outcome Measures:** Route-learning task; Sketch map test; Map recognition test; Scene arrangement test.	1. On the task, mean error rates for immediate and delayed recall were higher in the TG than in the CG, but this difference was not significant (p=0.42). 2. On the task, mean scores were higher on the second (immediate) recall and the third (delayed) recall compared to the first (immediate) recall in both groups (p<0.001). 3. On the task, mean scores were higher on the second recall than on the third recall in both groups, but the difference was not significant (p=0.44). 4. No significant interactions between recall and environment were found. 5. Mean scores on the scene arrangement test were significantly higher in the CG than in the TG (p=0.01). 6. Mean scores on the sketch mapping test were higher in the CG than in the TG, but this difference was not significant (p=0.07). 3. Mean scores on the map recognition test were the same in both groups (p=0.83).

Discussion

A 2013 RCT found that those who received virtual reality memory training showed a significant improvement in immediate recall of tasks and event-based performance (Yip & Man, 2013). Although the control group saw no improvements on items of memory evaluation there were no significant differences between groups on measures of community integration (Yip & Man, 2013). Sorita et al. (2013) found that practicing a route-learning task in a real urban environment or in a virtual stimulation of that environment showed similar improvements in route recall, suggesting that VR training improvements in functional tasks may be due to repetition and not the presented medium. Dahdah et al. (2017) also found that multiple Stroop tasks in VR environments resulted in improved performance on parts of those tasks. Virtual reality has been found to improve more than just memory as well, in an older RCT by Grealy et al. (1999), not only did individuals receiving VR exercise significantly improve on visual learning abilities, they also improved on reaction time.

Conclusions

There is level 4 evidence that virtual reality (VR) training may improve learning performance post ABI, even in the presence of distractions.

There is level 2 evidence that virtual reality training combined with exercise may be promising for improving memory outcomes and has a positive impact on visual and verbal learning when compared to no treatment.

There is level 2 evidence that virtual reality training may be superior to reading skills training at improving immediate and general components of memory for those with an ABI.

There is level 2 evidence that the format of route learning (either real or virtual reality based) does not significantly impact any improvements in memory as a result of route learning strategies for those with an ABI.

Virtual reality programs may enhance the recovery of memory, learning, but there is currently limited evidence supporting the use of virtual reality programs. The evidence is unclear as to which specific programs benefit memory rehabilitation and whether or not they are superior to manual training therapies.

6.2.1.1.2 Internal Memory Strategies

The following studies examined how different cognitive strategies could be used to enhance learning and memory following an ABI.

Table 6.17 The Effect of Internal Strategies on Learning and Memory Post ABI

Author Year Country Research Design PEDro Sample Size	Methods	Outcome
Grilli & McFarland (2011) United States RCT Crossover PEDro=4 N=12	**Population:** Mean age=49.42yr; Gender: Male=5, Female=7. **Intervention:** Participants were either instructed to self-imagine participation in a memory trivia game or rehearse the information they wanted to remember out loud during memory training trials. **Outcome Measures:** Prospective memory, neuropsychological functioning (executive functioning).	1. There was a significant between groups difference, where self-imagination instruction improved prospective memory (p<0.01). However, the proportion of questions answered correctly did not differ significantly between groups. 2. A Pearson correlations test showed that performance in the self-imagination condition was not significantly correlated to memory or executive functioning.
Bourgeois et al. (2007) USA RCT PEDro=2	**Population:** TBI patients: Mean Age: 41.5yr; Gender: male=24, female=14; Mean Time Post-Injury: 11.3yr. **Intervention:** Participants were randomized to receive either Spaced Retrieval (SR) training (n=22) delivered over the telephone or didactic strategy instruction	1. Those in the SR group showed significant improvement in goal mastery compared to the SI group (p<0.05). This was maintained at the one-month post intervention. 2. Results on the CDS showed both groups

Author Year Country Research Design PEDro Sample Size	Methods	Outcome
N=38	(DSI) (n=16). Participants in both groups identified three memory-related goals to master. **Outcome Measures:** Goal Mastery, Cognitive Difficulties Questionnaire (CDS).	having fewer significantly difficulties following treatment ($p<0.001$; $p<0.005$). 3. There were no significant between-groups differences in participant reports of generalized strategy use or reported memory problems at either time-point ($p>0.05$).
Kaschel et al. (2002) Germany RCT PEDro=6 N=27	**Population:** *Pragmatic Group (N=15)*: Mean age=36.6yr; Gender: Male=12, Female=3. *Imagery Group (N=11):* Mean age=41.9yr; Gender: Male=9, Female=2. **Intervention:** Individuals were assigned to either imagery-based training (experimental), or pragmatic-based training (control) for 10 weeks, 3 times a week. Individuals were assessed at baseline, immediately following treatment conclusions, and at 3-months follow-up. **Outcome Measures:** Concentration endurance, Wechsler Memory Scale (WMS), Rivermead Behavioral Memory Test (RBMT), Appointments test, Memory Assessment Clinics Rating Scales (MAC).	1. There was a significant effect of time for the assessment of concentration endurance with both groups significantly improving over time ($p<0.05$). No other significant measures were found for concentration endurance. 2. There were no significant differences between groups on the WMS. 3. For the RBMT, only a significant effect of time was observed ($p<0.05$). A specific subset of the RBMT for logical memory showed a significant group ($p<0.01$) and interaction effect ($p<0.05$) indicating that those in the imagery condition had improved logical memory. 4. When assessing ability to recall multiple appointment times, a significant effect of group ($p<0.05$), and time ($p<0.01$) was observed with individuals in the imagery performing better. 5. On the MAC scale for relative's rating of memory problems, there were significant interactions at all time points ($p<0.05$), and a significant effect of time ($p<0.05$) indicating that the self-imagery group had greater gains in memory according to relative's ratings compared to the pragmatic group.
Milders et al. (1995) Netherlands RCT PEDro=5 N=31	**Population:** Closed Head Injury (CHI); *Strategy Group (n=15)*: Mean Age=42.4yr; Mean Time Post-Injury=10.4yr; *Pseudo Group (n=8)*: Mean Age=35.6yr; Mean Time Post-Injury=12.4yr; *No-Treatment Group (n=8)*: Mean Age=37.7yr; Mean Time Post-Injury=12.9yr; *Healthy Control (n=13)*: Mean Age=41.1yr **Intervention:** 4yr follow-up to Berg et al. (1991). **Outcome Measures:** Four-choice Reaction Time Task, Distraction Reaction Time Task, 15-Words Test, Face-Name Learning, Shopping Lists.	1. Standardized memory sum scores at long-term follow-up were significantly lower in the three patient groups than in the normal control group ($p<0.05$). 2. Pseudo-rehab group improved significantly ($p<0.05$) in memory from post-training to long-term follow-up; such improvements were not seen in any other groups. 75% of patients in the pseudo group improved compared to 20% in the strategy group and 37.5% in the no-treatment group. 3. Reaction time scores did not differ significant between groups at follow-up ($P=0.08$).
Twum and Parente (1994) USA RCT PEDro=3	**Population:** TBI; Mean Age=21yr; Time Post Injury>6mo. **Intervention:** Patients were randomized into one of four treatment groups: 1) No Imagery/No Verbal Labeling (control); 2) No Imagery/ Verbal Labeling; 3)	1. MANOVA analysis revealed an overall significant main effect of mental imagery instructions ($p<0.0001$) and a main effect of verbal labeling instructions on the VisPA ($p<0.0001$).

Author Year Country Research Design PEDro Sample Size	Methods	Outcome
N=60	Imagery/No Verbal Labeling; and 4) Imagery /Verbal Labeling. Verbal labeling and imagery instructions were given through Verbal Paired Associated (VerPA) and Visual Paired Associated (VisPA) tasks, respectively. **Outcome Measure:** VerPA and VisPA tasks.	
Berg et al. (1991) Netherlands RCT PEDro=5 N=39	**Population:** Closed Head Injury (CHI); *Strategy Group (n=17)*: Mean Age=36yr; Mean Time Post Injury=5.3yr. *Pseudo Group (n=11)*: Mean Age=33yr; Mean Time Post Injury=6.3yr. *No-Treatment Group (n=11)*: Mean Age=35yr; Mean Time Post-Injury=6.8yr. **Intervention:** Individuals were randomly assigned to one of three groups: strategy rehabilitation, pseudo-rehabilitation, or no-treatment. The strategy rehabilitation group had individualized training targeting to the identified memory problems (1hr, 3x/wk for 6wk). Daily homework was administered to augment the benefits of rehabilitation. The pseudo-rehabilitation ("drill and practice") group participated in sessions consisted of memory tasks and games that were practiced in the laboratory and at home. The no-treatment group received no training. **Outcome Measures:** Four-choice Reaction Time Task, Distraction Reaction Time Task, 15-Words Test, Face-Name Learning, Shopping Lists.	2. No single effect of strategy training was found with respect to reaction time tasks post-training. 3. While no significant effect of pseudo-training was found, strategy training had significant positive effects on all memory performance measures (memory sum score: p=0.011; acquisition score: p=0.038; delayed recall score: p=0.004), particularly at the final follow-up.
O'Neil-Pirozzi et al. (2010b) USA Prospective Control Trial N=94	**Population:** TBI; *Experimental Group*: Mean Age=47.3yr; Mean Time Post-Injury=11.8yr; *Control Group*: Mean Age=47.0yr; Mean Time Post-Injury=13.4yr **Intervention:** Participants in the experimental group were trained to use Internal Memory Strategies (I-MEMS; n=54); the intervention consisted of 12 90-min sessions, held 2×/wk for 6 wk. It included memory education and emphasized internal strategy acquisition to improve memory function from encoding, storage and retrieval perspectives; the control group (n=40) consisted of a convenience sample. **Outcome Measure:** Hopkins Verbal Learning Test-Revised (HVLT-R), Rivermead Behavioural Memory Test II (RBMT II). Patients were assessed on Week 1 (pretest), Week 7 (posttest 1), and Week 11 (posttest 2).	1. Pretesting revealed a significant difference between experimental and control groups on the HVLT-R only (p=0.02). 2. Individuals who had a severe TBI performed more poorly on the HVLT-R than those with moderate injuries. 3. Although those with a severe injury did not improve as much as those with a mild or moderate injury, they did improve more than those in the control group at both posttest 1 (p=0.0002) and posttest 2 (p<0.0001). 4. Similar to what was found with HVLT-R assessments, severe injury predicted worse RMBT II scores than moderate injury. 5. RBMT II scores in the I-MEMS groups revealed significant improvements at both posttest 1 (p=0.045) and posttest 2 (p=0.0013) relative to control. 6. Overall memory performance was improved for all those in the experimental group compared to the control group.
Manasse et al. (2005) USA Case Series N=5	**Population:** TBI: Age Range: 29-48yr; Gender: male=3, female=2; Time Post-Injury: 1-29yr. **Intervention:** Subjects were shown pictures of individuals they interacted with daily and asked to identify them. **Traditional treatment**: To assist	1. **Traditional treatment:** results indicate that 2 of the 5 subjects mastered 6 names during treatment, 1 of the 5 mastered 3 names and 4 of the 5 mastered one of the names. 2. **Real-world treatment:** During the real-world

Author Year Country Research Design PEDro Sample Size	Methods	Outcome
	subjects in memory recall, pictures were paired with an imagery statement. There were 9 (3 weeklies over a 3-week period) one on one training sessions to assist the individuals with face name recognition. **Real-world treatment:** Following the third week, "real-world" treatment was begun. During the next 15 days, 2 interactions were performed each day with 2 hours separating the interactions. Researchers recorded the subjects' spontaneous use and knowledge of the staff's name. **Outcome Measures:** Name recall.	cueing condition only 2 names were consistently used by each subject. 3. Improved name learning was seen regardless of the cueing strategy.
Tailby & Haslam (2003) Australia Pre-Post N=24	**Population:** Head Injury=12, CVA=6, Hypoxia=3, Other=3. *Severe memory impairment group (n=8)*: Mean Age=43yr. *Moderate memory impairment group (n=8)*: Mean Age=43.8yr. *Mild/no memory impairment group (n=8)*: Mean Age=37.5yr. **Intervention:** 3 groups were formed based on Verbal Memory Index (VMI) on the Wechsler Memory Scale-III. All participants were tested in 3 conditions: errorful (EF), standard errorless (examiner-generated; EL-E) and self-generated errorless (EL-S). For training, 96 words of 5-6 letters were used over 2 sessions. Following the learning tasks, memory was tested explicitly and implicitly 5 and 30 min after the study phase, generating 6 scores for each learning condition. **Outcome Measures:** Verbal Memory Index (VMI).	1. Cued recall performance following EL-S learning was significantly better than standard errorless learning (EL-E) conditions ($p<0.0001$). 2. Level of priming did not differ significantly between groups ($p>0.05$). 3. Memory performance was significantly better following EL-E activity ($p<0.0001$) compared to EF. 4. A significant effect of severity was found ($p<0.005$) for the standard EL-E conditions; mild and moderate groups performed significantly better than severe group (defined by VMI: $p<0.0001$); significant effect of severity was also found for the EF condition ($p<0.001$).
Sumowski et al. (2014) USA Pre-Post N=10	**Population:** Severe TBI=10; Mean Age=42.8 yr; Gender: Male=6, Female=4; Mean Time Post Injury=8.4 yr. **Intervention:** Participants studied 48 verbal paired associates (VPAs) divided into 3 learning conditions: massed restudy (MR), spaced restudy (SR), and retrieval practice (RP). MR is similar to cramming, whereas SR is distributed learning. RP was similar to SR; however, re-exposure trials were framed as cued recall tests. Recall of VPAs was done at 30 min post intervention, and at 1 wk. Participants performed all 3 methods of learning. **Outcome Measure:** Recall of VPAs.	1. Participants recalled 46.3% of VPAs learned through RP compared with 12.5% through MR ($p<0.0001$), and 15% through SR ($p=0.002$). 2. SR did not result in better memory than MR ($p=0.0555$). 3. At 1wk, participants recalled 11.3% in the RP group compared to 0.0% in the MR ($p=0.004$), and 1.3% in SR ($p=0.011$). Again, SR and MR did not differ from each other ($p=0.343$).
Potvin et al. (2011) Canada PCT N=30	**Population:** TBI; *Rehabilitation Group (n=10)*: Mean Age=35yr; Gender: Male=7, Female=3. *Control Group (n=20)*: Mean Age=30.90yr; Gender: Male=11, Female=9. **Intervention:** Participants were assigned to either prospective memory (PM) rehabilitation programme or the standard neuropsychological interventions group (control). PM rehabilitation was based on the learning of visual imagery techniques. **Outcome Measure:** Test Ecologique de Memoire Prospective (TEMP), Visual Discrimination Task, Semantic Association Task, Letter Visualization Task,	1. The experimental group performed significantly better on the TEMP post PM training than the control group ($p<0.05$). 2. During the learning phase, cued recall improved for those in the experimental group, although this improvement was not found to be significant. 3. Participants who took part in the rehabilitation program improved their performance on the PM experimental task ($p<0.05$).

Author Year Country Research Design PEDro Sample Size	Methods	Outcome
	Digit Symbol, Cancellation Task, Trail Making Test A & B, Brown-Peterson Task, Digit Span, Sullivan Logical Memory, Rey Auditory Verbal Learning Test, Brief Visuospatial Memory Test, Semantic Verbal Fluency, Mazes, Stroop Interference and Flexibility, CAPM (relative and participant versions).	4. No significant group effects were found for any neuropsychological tests, except with the digit symbol test ($p<0.05$). 5. Self-evaluated PM failures was significantly lower post-test in the rehabilitation group ($p<0.05$) but not the control group.
Grilli & Glisky (2013) USA Pre-Post N=30	**Population:** *Patient Group*: TBI=13, ABI=2; Mean Age=51.3yr; Gender: Male=7, Female=8. *Healthy Control (n=15):* Mean Age=50.7yr; Gender: Male=7, Female=8. **Intervention:** Participants were exposed to five intentional coding conditions over two days. Controls did all five in one day. For each trial a word was on the screen for 10sec. A sentence specifying the task (condition) would appear above the target word. The conditions were: baseline, semantic elaboration, semantic self-referential processing, episodic self-referential processing, and self-imagining. **Outcome Measure:** Immediate free-recall test.	*only results for the TBI group are reported 1. For the patient group, self-imagining showed better free recall than baseline ($p<0.001$), semantic elaboration ($p<0.001$), episodic self-referential processing ($p<0.001$), and semantic self-referential processing ($p<0.05$). 2. Self-referential processing enhanced free recall more than episodic self-referential processing ($p<0.05$). 3. Semantic elaboration and episodic self-referential processing showed better free recall than scores attained at baseline ($p<0.05$, $p<0.01$, respectively). 4. Self-descriptive trait adjectives were recalled more than non-self-descriptive trait adjectives among only those in the self-imagining ($p<0.05$) and semantic self-referential processing conditions ($p<0.05$).
Sumowski et al. (2010) USA Case-Control N=28	**Population:** Mean Age of TBI=38.4yr; Etiology of injury: motor vehicle accidents (n=9), falls (n=2), sports injuries (n=2), and assault (n=1). Condition: TBI=14, Control=14. **Intervention:** Examining the effects of retrieval practice in delayed memory recall than simple restudy. Using a verbal paired associate paradigm examined recall abilities between controls and TBI patients. **Outcome Measures:** Delayed cue recall test.	1. A significant learning condition by group interaction was discovered ($p<0.001$). 2. Healthy controls benefited from spaced restudy over massed restudy ($p<0.001$). 3. Both groups greatly benefited from retrieval practice over massed and spaced restudy ($p<0.001$, $p=0.23$).
Scheffft et al. (2008) USA PCT N=20	**Population:** Mean Age: 31.8yr; Gender: male=13, female=7; Condition: TBI **Intervention:** **Study 1: Read condition**: words were presented in pairs-1 pair per card, which participants were asked to read aloud. **Generate condition**: participants were shown one word on the card with the first letter of second word and asked to read aloud the words as soon as they knew the second word. The first recall test was given immediately after the presentation of the 50-word pairs, followed by the recognition memory test. Free recall test had patients write down as many of the second words from each pair that could be remembered. **Recognition Test:** 50 items corresponding to the appropriate input list and each item was composed of 2 previously unseen distractor words and 1 target word from the learning task. Word	**Study 1**: 1. Self-generation encoding procedures improved recognition memory test performance, but not free recall, compared with the didactic presentation. **Study 2**: 1. Self-generation strategy improved cued recall, but not free recall compared with the didactic condition. 2. Study results also indicated that cued recall was also important as it was found to be effective when presented with the first word of the word pair.

Author Year Country Research Design PEDro Sample Size	Methods	Outcome
	pairs were presented in the same order at testing as they had been presented during the learning trials. **Population:** Mean Age: 34.3yr; Gender: male=18, female=2, Condition: TBI. **Study 2:** Both the read and generate conditions were identical to study 1; however, here there was no recognition test. Patients were given a cued recall trail, where each word pair association rule was provided as a cue for memory and a cued recall trail where the first word in the pair was presented. Free recall test had participants write down as many of the second words from the pair they could remember. For the cued recall with rules test they were given a sheet of paper with the title on it and one example of each rule. They were then asked to write down as many of the second words they could remember.	
Hillary et al. (2003) USA Case Series N=20	**Population:** Age Range: 18-55yr; Gender: male=16, female=4; Mean Time Post-Injury: 4.1yr; Condition: moderate to severe TBI. **Intervention:** Examining if learning in TBI patients can be improved using spaced repetitions of a procedure compared to consecutive presentations of a procedure. A list of 115 words were chosen for recall, words were presented either once (single condition), twice consecutively (massed condition), or twice with 11 words between presentations (spaced condition). **Outcome Measures:** Immediate and Delay Recall; Delay Recognition Trials, neuropsychological tasks.	1. Spaced words were more likely to be recalled during the immediate recall than massed words ($p=.018$). 2. On the delayed recall spaced words were more likely to be correctly recalled than massed words or once presented words during delayed recall performance ($p<0.001$). 3. On the recognition performance test, individuals were able to correctly identify spaced words over massed ($p=0.001$) or once presented words ($p=0.017$). 4. Significant main effect for study condition on immediate recall in the neuropsychological tasks ($p<0.001$).
Milders et al. (1998) Netherlands Prospective Control Trial N=26	**Population:** Closed Head Injury (CHI)=13; Healthy Controls=13. *CHI Group*: Mean Age=39yr; Mean Time Post Injury=5yr. **Intervention:** Individuals with TBI completed exercises with standardized instructions that help make the new name more meaningful to the learner (8, 60-90min sessions over 4mo). Participants were assessed at baseline (3x) and 1wk and 6mo after training. **Outcome Measures:** Name Learning Test, Name-Occupation-Town Learning Test, Famous Faces Naming Test, Digit Span Forwards, Auditory Verbal Learning Task.	*only results for the TBI group are reported 1. A main effect for the patient's group was found for the Name-Occupation Town Test ($p<0.001$). 2. Performance on the name learning test for the patient's group from pre-to post training (meaningful names= 12.8 ± 4.6 to 14.0 ± 3.6; meaningless names=11.6 ± 3.9 to 11.7 ± 3.2). 3. There were improvements on the Name-Occupation-Town Learning Test in the patient group (names= 16.8 ± 7.7 to 21.6 ± 7.2; Occupations + town= 22.4 ± 9.4 to 23.5 ± 8.2).
Thoene & Glisky (1994) Germany PCT N=12	**Population:** Mean age=45.58yr; Gender: Male=6, Female=6; Mean time post-injury=7.38yr. **Intervention:** Individuals attempted to learn the names associated with 4 faces in 3 conditions (mnemonic, vanishing cues, and video). Mnemonic trials consisted of associating a face with an elaborate verbal association. The video condition consisted of the 'face subject' introducing themselves via video to the participant. The vanishing cues condition	1. There as a significant effect of condition where the only condition to reach the criterion threshold was the mnemonic condition ($p=0.001$). Post hoc tests confirmed that individuals required fewer trials in the mnemonic condition to reach criterion ($p=0.017$).

Author Year Country Research Design PEDro Sample Size	Methods	Outcome
	consisted of cueing the individual to remember the name during training sessions by cueing them with letters from the target name. **Outcome Measures:** Naming errors: Omission errors, other-set intrusions (information from another condition), same-set intrusions, other errors in naming, reaching criterion threshold, incidental recall (information not related to names).	2. While participating in the vanishing cues condition, individuals required less cues to remember target names over time. 3. There were significant differences between conditions for omission made, with the mnemonic group making significantly less (p=0.000). 4. There were significantly fewer other-set intrusions in the mnemonic group, compared to the other groups (p=0.04). 5. There were significantly fewer same-set intrusions in the mnemonic condition than other conditions (p=0.01). 6. The incidental recall of the target's professions was significantly higher in the video condition compared to other conditions (p=0.04).

PEDro = Physiotherapy Evidence Database rating scale score (Moseley et al., 2002a).

Discussion

A variety of internal memory strategies exist which attempt to remediate memory deficits following an acquired brain injury. As a result of the breadth of strategies attempted and evaluated, few studies overlap in methodology and protocol limiting the conclusions that can be made about each intervention.

Potvin et al. (2011) used one of the more common strategies; visual imagery techniques. Following visual imagery instruction, the scores on the Test Ecologique de Memoire Prospective significantly improved for those in the visual imagery group, this group also reported significantly fewer prospective memory errors and depression. Prospective memory is an area that has been found to be positively affected by more than one imagery technique. Another RCT found that self-imagery significantly improved prospective memory compared to information rehearsal (Grilli & McFarland, 2011). Imagery techniques in general have been found to be effective for improving general memory (Twum & Parente, 1994), as well as specific areas of memory like logical memory (Kaschel et al., 2002). Overall, there is strong evidence to support the use of imagery techniques to improve memory. One study used self-imagery in combination with a variety of other encoding techniques to determine its efficacy against other encoding strategies such as semantic elaboration (Grilli & Glisky, 2013). It was found that those in the self-imagining condition showed better free recall than the control condition, but also recalled more self-descriptive adjective words than the other control and experimental conditions (Grilli & Glisky, 2013).

Another common memory strategy is retrieval practice. A variety of different retrieval strategies have been studied, such as spaced retrieval, massed retrieval, and cued retrieval (Sumowski et al., 2014). The use of retrieval strategies has been shown to significantly improve goal mastery (Bourgeois et al., 2007), delayed recall (Hillary et al., 2003; Sumowski et al., 2010), and immediate recall (Hillary et al., 2003). Bourgeois et al. (2007) found that compared to didactic strategy instruction, spaced retrieval significantly improved goal mastery; however, both groups achieved significant improvements in memory and memory errors. In a follow-up study to Berg et al. (1991), which found significant improvements on all memory measures as a result of individual strategies, Milders et al. (1995) found that at four-year follow-up the group which experienced 'drill and practice" retrieval strategies had the best long-term memory outcomes. Although a general trend has shown spaced retrieval and cued retrieval to be effective, it should be noted that the highlighted studies did not overlap in terms of their application of this strategy. Multiple studies have shown that massed retrieval or "cramming" is not an effective strategy for improving memory (Hillary et al., 2003; Sumowski et al., 2010).

Strategies which use multiple encoding techniques have also been found to be effective. Milders et al. (1998) examined performance on a name learning task by increasing the meaningfulness of people's names with various strategies (e.g. when learning a new name-face association try to think of an occupation or object with the same name or a famous person with a similar name). This was shown to improve memory and recall (Milders et al., 1998). Also, learning procedures were more effective on one task (where subjects were required to learn the name-occupation-and town) compared to the other two tasks (famous-faces or name learning). Twum and Parente (1994) randomly assigned 60 patients with a TBI into one of four groups (one control and three mnemonic strategy groups) counterbalanced. The research demonstrated improved performance for subjects who were taught a strategy (either verbal labeling or visual imagery, or both) while learning paired-associations. Treatment groups showed greater efficiency in learning and greater delayed recall information. This conclusion is supported by other studies which have found general improvements in memory when combining multiple encoding cues such as visual imagery and verbal/written cues (Manasse et al., 2005). In a final study examining encoding, individuals were taught word association pairs and found that when primed with the first word of the pair, individuals were able to recall the second word more effectively (Schefft et al., 2008).

The remaining interventions have been explored in limited studies. Thoene and Glisky (1995) using a case series design also showed enhanced performance following the use of a mnemonic strategy (verbal elaboration and visual imagery) compared to vanishing cues and/or video presentation during paired associations. A pre-post study examined the type of errorless learning to take place (self-generated or examiner generated) and found that self-generated errorless learning resulted in significantly higher recall (Tailby & Haslam, 2003). However, examiner errorless learning was observed to be better than errorful learning. Lastly, an interaction effect was seen with regard to injury severity such that those of a mild to moderate ABI responded better to treatment than those with a severe injury (Tailby & Haslam, 2003). A combination of internal memory strategies was also found to be effective for improving memory compared to a convenience sample of controls (O'Neil-Pirozzi et al., 2010a). Similar to the previous study, it was seen that those with mild to moderate ABIs gained the most from treatment, while those with a severe injury were not able to perform as well over all (O'Neil-Pirozzi et al., 2010a).

Conclusions

There is level 1b evidence to support self-imagination as an effective strategy to improve memory compared to standard rehearsal for those with an ABI.

There is Level 2 evidence to support that spaced retrieval training is an effective memory strategy when compared to massed retrieval or rehearsal in ABI populations.

There is level 2 evidence that strategies that utilize methods of multiple encoding, compared to strategies which only use singular methods, are more superior for improving memory post ABI.

There is level 4 evidence that errorless learning is more effective than errorful learning when it comes to improving memory in ABI populations.

Internal strategies such as self-imagination, spaced retrieval and rehearsal, and multiple encoding are effective for improving memory following an ABI.

6.2.1.2 Learning and Memory Training Programs

Following a brain injury, one of the most persistent problems are memory deficits (Hasegawa & Hoshiyama, 2009). Although the literature examining the efficacy of memory programs is limited, there is some support for training that stresses external memory strategies. Again the support for these programs is limited as many individuals post injury neglect their devices or simply stop using them (O'Neil-Pirozzi et al., 2010a).

Table 6.18 The Effect of Memory Retraining Programs on Memory Post ABI

Author Year Country Research Design PEDro Sample Size	Methods	Outcome
Lesniak et al. 2018 Poland RCT PEDro=7 N=65	**Population:** *Group Therapy (N=18):* Mean age=41.3yr; Gender: Male=11, Female=7; Mean time post-injury=15.2mo. *Individual Therapy (N=23):* Mean age=39.6yr; Gender: Male=17, Female=6, Mean time post-injury=11.6mo. *No Therapy (N=20):* Mean age=42.2yr; Gender: Male=13, Female=7; Mean time post-injury=10mo. **Intervention:** Participants were assigned to either the individual therapy group (IT), the group therapy group (GT), or the no therapy group (NT). Individuals were assessed pretreatment, immediately post treatment (3 weeks), and at 4-month follow-up. **Outcome Measures:** Cambridge Neuropsychological Test Automated Battery (CANTAB), Rivermead Behaviroal Memory Test (RBMT)	1. All groups saw a significant improvement over time on the RBMT (p<0.05). There were no significant differences between posttreatment and follow-up in any group. Only the GT group saw a significant difference between pretreatment and follow-up (p<0.05). 2. On the Pattern Recognition Memory subset of the CANTAB both the IT and the NT groups has significantly higher scores (p=0.016, p=0.015) respectively. Only the IT group maintained this difference at follow-up (p=0.002). 3. The IT group was the only group to see a significant difference on the spatial span (p=0.031) and rapid visual processing (p=0.024) subsets of the CANTAB. 4. No other significant differences were found.
Lindelov et al. (2017) Denmark RCT PEDro=7 N=68	**Population:** TBI=34, Stroke=20, Other=12, NA=2. *Group A (n=27)*: Mean Age=45.2 yr; Gender: Male=12, Female=15; Mean Time Post Injury=5 yr. *Group B (N=22)*: Mean Age=47.0 yr; Gender: males=8, females=25; Mean Time Post Injury=6.5 yr. *Control Group (n=19)*: Mean Age=54.1 yr; Gender: males=8, females=11; Mean Time Post Injury=7 yr. **Intervention:** Participants were randomly assigned to Group A or Group B; Control group was recruited separately and received no intervention. In Phase 1, Group A received the first version of a targeted hypnosis procedure	1. In Phase 1, there was significantly more improvement in Group A compared to Group B for WMI (Bayes factor=342) and TMT (Bayes factor=37.5). 2. After the break, the WMI and MT showed no significant differences for either groups compared to before the break. 3. In Phase 2, Group B crossed over to the targeted intervention and showed significant improvements in WMI (Bayes factor=535) and TMT (Bayes factor=72813). Group A showed a small improvement for WMI (Bayes factor=1.5) and TMT (Bayes factor=30).

Author Year Country Research Design PEDro Sample Size	Methods	Outcome
	(improving brain injury or working memory-relating abilities) and Group B received a non-targeted hypnosis procedure (4 weekly 1 h sessions). After a 7-wk break, Phase 2 occurred, with Group A receiving a second version of a targeted hypnosis procedure and Group B receiving the first version of a targeted hypnosis procedure. **Outcome Measures:** Working Memory Index (WMI), B-A Trail Making Index (TMT).	4. From baseline to last test, there were no significant difference in improvements between Group A and Group B for WMI and TMT.
Chiaravalloti et al. (2016) USA RCT PEDro=9 $N_{Initial}$=69 N_{Final}=53	**Population:** TBI. *Treatment Group (TG, n=35):* Mean Age=37.17 yr; Gender: Male=27, Female=8; Mean Time Post Injury=120 mo; Mean GCS=4.83. *Control Group (CG, n=34):* Mean Age=40.68 yr; Gender: Male=24, Female=10; Mean Time Post Injury=102 mo; Mean GCS=5.0. **Intervention:** Participants were randomized to receive the modified Short Memory Technique (TG) or conventional therapy (CG) in 10 sessions over 5 weeks. Participants in the TG were randomized to receive 5 monthly booster sessions (BS) or control sessions (CS) after treatment. Outcomes were assessed before and after treatment, and at 6 mo follow-up. **Outcome Measures:** California Verbal Learning Test (CVLT); Memory Assessment Scales, Prose Memory (MAS-PM); Rivermead Behavioural Memory Test (RBMT).	1. On the CVLT, there was no significant difference between groups after treatment (F=0.686, p>0.05). 2. On the MAS-PM, the TG showed significantly greater improvement than the CG after treatment (F=4.45, p<0.025). 3. On the MAS-PM, 49% of the TG showed a significant improvement after treatment compared to 18% of the CG (p=0.006). 4. On the MAS-PM, 23% of the TG showed a reliable positive change after treatment compared to 9% of the CG. 5. On the MAS-PM, there was no significant difference between the TG and the CG in performance at follow-up (p>0.05). 6. On the MAS-PM, there was no significant difference between participants in the TG who received BS or CS (p>0.05). 7. On the RBMT, significantly more participants in the TG demonstrated improvement on the ‘hidden belonging task’ after treatment than participants in the CG (p=0.025).
Sandry et al. (2016) USA Post Hoc Analysis: Chiaravalloti et al. (2016) N=69	**Population:** See above. **Intervention:** See above. **Outcome Measures:** Working memory capacity (WMC); Long-term memory percent retained (LTMPR).	1. Main effects of group (TG vs CG) and capacity (high vs low) were not significant (p>0.050), but the interaction between the two variables was significant (p=0.008). 2. WMC and LTMPR were significantly positively correlated in the TG (p<0.001) but not in the CG (p=0.220). 3. LTMPR change scores did not differ as a function of group (p=0.450). 4. LTMPR change scores were not significantly correlated with other cognitive domains (p>0.360).
Novakovic-Agopian et al. (2011) USA RCT Crossover PEDro=5 N=16	**Population:** TBI=11, Stroke=3, Other=2: Mean Age=50.4 yr; Gender: Male=7, Female=9; Time Post Injury Range=1-23 yr. **Intervention:** Participants were randomized to 5 wk interventions consisting of a goals training program (n=8) or an educational instruction group (n=8). Goal training focused on	1. At the end of wk 5 participants in the goals-edu group showed significant improvement on measures of attention and executive function from baseline (p<0.0001), while the edu-goals group showed no change or minimal change (p>0.050).

Author Year Country Research Design PEDro Sample Size	Methods	Outcome
	mindfulness-based attentional regulation and goal management strategies for participant-defined goals. Educational training was didactic instructional sessions about brain injury. At the end of 5 wk, participants were switched to the other intervention. All participants were assessed at baseline, Week 5 and again at Week 10. **Outcome Measures:** Auditory Consonant Trigrams, Letter Number Sequencing (working memory); Digit Vigilance Test (sustained attention); Stroop Inhibition Delis-Kaplan Executive Function System (Inhibition); Trails B, Design Fluency-switching (mental flexibility), Hopkins Verbal Learning Test-Revised, Brief Visual Memory Test-Revised.	2. The goals-edu group had significantly greater improvements than the edu-goals group on the following at wk 5: working memory (*Mean* 1.12 vs -0.12, p<0.0001); mental flexibility (*Mean* 0.64 vs 0.04, p=0.009); inhibition (*Mean* 0.62 vs 0.04, p=0.005); sustained attention (*Mean* 0.96 vs 0.27, p=0.01); learning (*Mean*=0.51 vs 0.08, p=0.020); and delayed recall (*Mean* 0.39 vs -0.27, p=0.01). 3. At wk 10, the edu-goals group significantly improved compared to wk 5 on: attention and executive function (0.79 vs 0.03, p<0.0001); working memory (1.31 vs -0.12, p<0.0008); mental flexibility (0.66 vs 0.04, p<0.0008); inhibition (0.50 vs 0.04, p=0.010); sustained attention (0.44 vs 0.27, p=0.010); memory (0.609 vs -0.10, p=0.020); learning (0.66 vs 0.08, p=0.050); and delayed recall (0.55 vs -0.27, p=0.020). 4. Those in the goals-edu group who had completed the training session were able to maintain their gains and there were significant improvements in attention and executive function (p<0.040) and working memory (p<0.020).
Shum et al. (2011) Australia RCT PEDro=7 N=45	**Population:** TBI patients: Age Range=19-57 yr; Gender: male=37, female=8; Mean Glasgow Coma Score: 6.25, Mean time since injury=273 day. **Intervention:** Participants were randomized to one of four treatment groups: self-awareness training, active control for self-awareness with training, compensatory prospective memory (PM) training, and active control for compensatory PM training. All interventions involved 8 weekly attendances (1.5 hr each). Participants were assessed at baseline and after intervention. **Outcome Measure:** Cambridge Prospective Memory Test (CAMPROMPT); number of valid diary entries; Comprehensive Assessment of Prospective Memory (CAPM); Sydney Psychosocial Reintegration Scale (SPRS).	1. All 4 groups showed no significant differences on the CAMPROMPT during the pre-intervention phase. 2. Following intervention, those with a self-awareness training component were not significantly different from those without on the change scores. 3. Groups with a compensatory training component were found to have a significantly larger change score than those without (p=0.007). 4. There was a significant increase in the number of participants who took notes (p=0.008). 5. Post intervention the groups with a compensatory training component were found to have larger change scores than those without (p<0.017). 6. Scores on the CAPM and SPRS were not significantly different among the 4 groups pre- or post-intervention.
Vas et al. (2011) USA RCT PEDro=6 N=28	**Population:** TBI: *Strategic Memory and Reasoning Training (SMART) Group* (n=14): Mean Age=39 yr; Gender: Male=9, Female=5; Mean Time Post Injury=16.71 yr. *Brain Health Workshop Group* (n=14): Mean Age=47 yr; Gender: Male=7, Female=7; Mean Time Post Injury=16.35 yr.	1. The SMART group had significantly greater TOSL scores compared to the control group post-training (SMART *Mean*=19.76, BHW *Mean*=13.69, p=0.030). 2. The SMART group had significant improvements in TOSL scores: post-training (*Mean*=19.76, p=0.007) and at 6-month follow-up

Author Year Country Research Design PEDro Sample Size	Methods	Outcome
	Intervention: Participants were randomly assigned to the SMART group or the BHW group. Participants received a total of 12 group sessions over an 8 wk period. The SMART group learned about strategies they could apply in their daily lives; homework was given at the end of each session. The BHW group sessions were designed to be information-based and reading assignments were given each week. Participants were assessed at baseline, post-training (3 weeks) and at 6-month follow-up. **Outcome Measure:** Test of Strategic Learning (TOSL); Working memory listening span task; Community Integration Questionnaire (CIQ); Wechsler Adult Intelligence Scale III (WAIS III).	(*Mean*=21.15, p=0.004) from baseline (*Mean*=14). 3. The SMART group had significantly greater improvements than the control group on the working memory listening span task post-training (SMART *Mean*=4.23, BHW *Mean*=2.59, p<0.001). 4. The SMART group had significant improvements post-training in the working memory listening span task (*Mean*=4.23, *p*=0.005) and at 6-month follow-up (*Mean*=4.96, P=0.0001) compared to baseline (*Mean*=2.76). 5. The SMART group had significantly greater improvements on CIQ compared to the BHW group (SMART *Mean*=18.73, BHW *Mean*=16.45, p=0.020). 6. The SMART group had significant improvements in the CIQ at the 6-month (*Mean*=19.88, p=0.010) follow-up from baseline (*Mean*=15.19). 7. Those in the SMART group showed significant improvement on 3 executive functions following training (inhibition: p=0.010; nonverbal reasoning: p=0.001; and cognitive flexibility: p=0.010) on the WAIS-III.
Zlotowitz et al. (2010) UK RCT PEDro=6 N=16	**Population:** TBI=5, Stroke=7, ABI=4; Mean Age=38.63yr; Gender: Male=11, Female=5; Mean Time Post Injury=4.44mo. **Intervention:** Participants were randomly assigned to either the modeling or moulding group. Participants were required to learn a sequence of 7 hand movements. The moulding condition involved a hand over hand technique and the modeling technique had the participant copy the experimenter's hand motions. **Outcome Measures:** Repeatable Battery for the Assessment of Neuropsychological Status (RBANS), Patients' recall of sequences.	1. From the total sample, the RBANS mean immediate memory subtest score was 80.81±20.39 and the standardized score for delayed memory was 73.94±20.86. 2. No significant differences were seen in accuracy between groups after the short delay (p>0.05); however, after the longer delay, accurate recall was significantly better after using the modeling technique compared to moulding condition (mean 2.63±1.23 vs 1.56±1.63, p=0.028).
Thickpenny-Davis et al. (2007) New Zealand RCT PEDro=5 N=14	**Population:** Mean age=32.75yr; Gender: Male=12, Female=2; Mean GCS=6.6. **Intervention:** Individuals were assigned to either a memory rehabilitation program or a waitlist control group. The memory program consisted of 8 sessions. Measures were taken at baseline, immediately following intervention, and at 1-month follow-up. **Outcome Measures:** California Verbal Learning Test (CVLT), Wechsler Memory Scale-Logical Memory (WMS-LM), visual paired associates (VPA), Integrated Visual and Auditory Continuous Performance Test (IVA-CPT), Memory in Everyday Life and Use of Aids and	1. Immediately following rehabilitation the memory rehabilitation group had significantly improved scores on the CVLT-long delay free subtest (p=0.007), WMS-LM delayed recall (p=0.009), used significantly more memory aids (p=0<0.001), and had significantly higher memory quiz scores (p<0.001). 2. When comparing immediately after rehabilitation to follow-up, there was a significant difference in VPA delayed recall scores (p=0.048). 3. Comparing baseline to 1-month follow-up scores there was a significant difference

Author Year Country Research Design PEDro Sample Size	Methods	Outcome
	Strategies Questionnaire, Behavioral indicators of memory impairment checklist, Memory Quiz, participant feedback questionnaire.	
Dou et al. (2006) China RCT PEDro=5 N=37	**Population:** TBI; Mean Age=38.07 yr; Gender: Male=27, Female=10; *Computer Assisted Memory Training Group (CAMG; n=13):* Mean Time Post Injury=270.15 d. *Therapist Administered Memory Training Group (TAMG; n=11):* Mean Time Post Injury=161.27 d. *Control Group (n=13)*: Mean Time Post Injury=226.77 d. **Intervention:** Patients were randomized to the CAMG, TAMG, or control group. Each group received memory training with similar content; however, it was delivered differently within groups (computer vs therapist). The control group received no training. Both treatment groups received 20 training sessions (45 min, approximately 6/wk for 1 mo). **Outcome Measure:** Neurobehavioural Cognitive Examination (NCSE), Rivermead Behavioural Memory Test (RBMT), Hong Kong List Learning Test.	1. Scores from the NCSE indicate that there was a significant increase in the TAMG (p=0.015) and the CAMG (p=0.020) on the memory subtest of each scale compared to the control group, but the two treatment groups were not significantly different from each other (p=0.256). 2. When looking at the results of the scores on the RBMT, there was only a significant difference between the CAMG and the control group (p=0.0001), as well as the TAMG and control (p=0.0001); there were no significant differences between the two treatment groups. 3. On the Hong Kong List Learning test, CAMG showed a significant positive change in encoding, storage and retrieval in the random and blocked arrangement of words (p<0.050).
Rath et al. (2003) USA RCT PEDro=2 N=46	**Population:** TBI: Mean Age=43.6 yr; Gender: Male=23, Female=37; Mean Time Post Injury=48.2 mo. **Intervention:** Patients were randomized into the innovative (n=32) or conventional (n=28) treatment groups. The innovative group received 24, 2 hr sessions focusing on emotional self-regulation and clear thinking. The conventional group received 24, 2-3 hr sessions focusing on cognitive remediation and psychosocial groups. **Outcome Measure:** Weinberg Visual Cancellation Test, Stroop Color–Word Task, FAS—Controlled Oral Word Association Test, Will-Temperament Scale, Visual Reproduction, Immediate and Delayed recall, Watson-Glaser Critical Thinking Appraisal, Wechsler Adult Intelligence Scale—III.	1. The innovative group showed significant improvements in visual memory immediate recall (p<0.001). 2. The conventional and the innovative group showed significant improvements: on logical memory recall (p<0.001), logical memory delayed recall (p=0.010), and visual memory delayed recall (p=0.010). 3. The conventional group had significant improvements in reasoning (p<0.050). 4. The innovative group had significant improvements in executive function (p<0.050); problem-solving self-appraisal (p=0.005); self-appraised clear thinking and emotional self-regulation (p<0.01); and observer ratings of roleplayed scenarios (p<0.005).
Eakman & Nelson (2001) United States RCT PEDro=5 N=30	**Population:** Mean age=29.6yr: Gender: Male=30, Female=0; Mean time post-injury=53.5 mo. **Intervention:** Participants were randomly assigned to receive either hands-on meatball making training, or verbal instruction only meatball making training, which consisted of a 10-step instruction process. **Outcomes:** Memory of steps involved in making meatballs.	1. The hands-on meatball group remembered significantly more steps for making meatballs than the verbal instruction group (p<0.001).

Author Year Country Research Design PEDro Sample Size	Methods	Outcome
Fasotti et al. (2000) Netherlands RCT PEDro=5 N=22	**Population:** TBI; *Experimental Group (n=12)*: Mean Age=26.1yr; Gender: Male=8, Female=4; Mean Time Post Injury=9.8mo. *Control group (n=10)*: Mean Age=30.1yr; Gender: Male=7, Female=3; Mean Time Post Injury=8.3mo. **Intervention:** Patients in the experimental group received Time Pressure Management (TPM) training (1hr, 2-3x/wk, 2-3wk). TPM training used videotaped short stories. The program was designed to increase awareness of errors and deficits, encourage the acceptance and acquisition of the TPM strategy, and emphasize strategy application and maintenance. The control group received concentration training (30min, 2-5hr/wk, 3-4hr). Patients were assessed 2wk prior to training, post-training, and at 6mo follow-up. **Outcome Measure:** Waterbed (WB) and Harvard Graphics (HG) tasks, Rey's 15-word test, Rivermead Behavioural Memory Test, Auditory Concentration Test, Paced Auditory Serial Addition Task, Visual Choice Reaction Time Task.	1. Training improved performances in both HG and WB tasks, but differences were not significant relative to control. 2. Scores on 2 of 3 standardized memory variables and all 3 attention variables increased significantly in the TPM group (p<0.05), whereas no memory variables and 1 of 3 attention variables increased significantly for the control group. 3. Follow-up (6 mo) data for 10 from the TPM group and 9 from the control group indicated that there was a significant time effect (p<0.05) but no significant group time interaction (p=0.23); this suggests that there still was a significant improvement after 6 mo but that this improvement could not be attributed specifically to the treatment or control training.
Sohlberg et al. (2000) USA RCT PEDro=8 N=14	**Population:** TBI=11, ABI=1, Other=2. *Attention Process Training (APT) Group (n=7)*: Mean Age=33.1 yr; Mean Time Post Injury=7.5 yr; *Control Group (n=7)*: Mean Age=38.1 yr; Mean Time Post Injury=1.6 yr. **Intervention:** Patients were randomized to receive either the APT training (treatment) or the brain injury education and supportive listening (control), in a cross over design. APT was 24 hr over 10 wk and the control group received 10 hr over 10 wk. All subjects worked directly with a therapist and assessed pre and post intervention. **Outcome Measure:** Trail Making Test, Paced Auditory Serial Addition Task (PASAT), Gordon Diagnostic Vigilance and Distraction, Controlled Oral Word Association Task (COWAT), Stroop Task, Attention Questionnaire.	1. Those in the APT group reported significantly more changes than the control group (0.91 and 0.58 respectively, p<0.050). 2. The effect of type of change was significant (p<0.0001); a greater number of memory/ attention changes were reported for the APT group, whereas more psychological changes were reported for the control. 3. Changes in PASAT scores corresponded with perceived cognitive improvement in the interview; changes in PASAT scores were greater for those who reported >2 cognitive changes (p<0.050). 4. Results of the PASAT, Stroop Task, Trail Making Test B, and COWAT also found that those with higher levels of vigilance had improved scores (p<0.010). 5. For the aforementioned tasks, there were also specific improvements in performance associated with APT that were greater than those associated with brain injury education (p<0.050).
Novack et al. (1996) USA RCT PEDro=5 N=44	**Population:** Severe TBI; *Focused Stimulation Group (n=22)*: Mean Age=28.7 yr; Mean Time Post Injury=5.9 wk. *Unstructured Stimulation Group (n=22)*: Mean Age=26.4 yr; Mean Time Post Injury=6.4 wk **Intervention:** Participants were randomly placed into a focused or unstructured	1. Analysis of primary outcome measures revealed no significant differences between the focused and unstructured stimulation groups, both at baseline and discharge. 2. There was a significant time effect with participants performing significantly better at

Author Year Country Research Design PEDro Sample Size	Methods	Outcome
	stimulation group. Patients in the focused group received hierarchical attentional learning training (30 min, 5 x/wk). Skills were not taught in a hierarchical or sequential fashion in the unstructured group. **Outcome Measure:** Digit Span and Mental Control subtests of Wechsler Memory Scale-Revised (WMS-R), computer-based simple and choice reaction time tests. *Secondary outcome measures*: Logical Memory I & II, Sentence Repetition, Judgment of Line Orientation, Trail Making A & B, Arithmetic subtest Wide Range Achievement Test-Revised, Visual imperceptions.	the time of discharge than on admission (p<0.0001). 3. There were no significant differences between the groups with respect to any secondary outcome measures studied.
Niemann et al. (1990) United States RCT PEDro=7 N=29	**Population:** *Attention Group (N=13)*: Mean age=28.9yr; Mean time post-injury=41mo. *Memory Group (N=13):* Mean age=34.3yr; Mean time post-injury=37.1mo. **Intervention:** Individuals were randomly assigned to either an attention training program or a memory training program. Both programs lasted 9 weeks and had two 2-hour sessions each week. **Outcome Measures:** Attention Test d2, Paced Auditory Serial-Addition Task (PASAT), Divided Attention test (DAT), Trail Making Test-B (TMT-B), Rey Auditory Verbal Learning Test (RAVLT), Block Span Learning Test (BSLT), Ruff 2 & 7 Test, Logical Memory Subtest (Wechsler Memory Scale) (WMS-LM), Ruff-Light Trail Learning Test (RLTLT).	1. There were no significant within-group differences on the Test d2, PASAT, DAT, RAVLTBSLT, Ruff 2 & 7 Tests, WMS-LM, or the RLTLT. 2. Significant within group differences were seen on the TMT-B for both the attentional (p<0.01), and memory (p<0.01) groups. 3. The attention group improved significantly more on the TMT-B compared to the memory group (p=0.05). 4. The attention group improved significantly more than the memory group on the Attention Test d2 (p=0.02). 4. No other significant differences were found.
Ryan & Ruff (Ryan & Ruff, 1988) United States RCT PEDro=8 N=20	**Population:** Mean age=32.85yr; Gender: Male=14, Female=6. **Intervention:** The experimental group received attention and spatial integration exercises, and memory retraining in addition to normal therapy. The control group received normal training. **Outcome Measures:** Benton Visual Retention Test (BVRT), Rey-Osterrieth Complex Figure Test (CFT), Taylor Complex Figure Test (TCFT), Selective Reminding Test (SRT), Ruff-Light Trail Learning Test (TLT), Wechsler Memory Scale (WMS), Logical Memory Subtest (WMS).	1. There were no significant differences between groups on any of the outcome measures. 2. A post-hoc analysis showed that those with mild cognitive impairment benefitted more from the intervention than those with moderate or severe cognitive impairment, but not significantly.
Holleman et al. (2018) Netherlands PCT N=75	**Population:** *Experimental Group (N=42):* Mean age=43.3yr; Gender: Male=27, Female=15; Mean time post-injury=7.9yr. *Control Group (N=33)*: Mean age=40.7yr; Gender: Male=20, Female=13; Mean time post-injury=6.9yr. **Intervention:** Participants were either assigned to the Intensive NeuroRehabilitation programme or the control group. The	1. There were no significant between group differences pre-intervention on any measures. 2. Following the intervention, the experimental group had significantly lower SCL scores indicating a reduction in overall symptoms (p=0.005). 3. On measures of neuropsychological functioning, the experimental group reported significantly

Author Year Country Research Design PEDro Sample Size	Methods	Outcome
	programme took place over the course of 16 weeks and consisted of 2 groups of 7 weeks of training with a 2-week break in between. Individuals had 5 hours of training 4 days a week in a group setting. **Outcomes:** Symptom checklist (SCL), Beck Depression Inventory-II (BDI-II), Hospital Anxiety and Depression Scale (HADS), Zelfbeeldenvragenlijst-trait (ZBV), Quality of Life in Brain Injury (QOLIBRI), Trail making test Part A, Stroop test, Wechsler Adult Intelligence Scale-III (WAIS-III), Rey Auditory Verbal Learning Test, Rivermead Behavioural Memory Test, Groninger Intelligentie Test 2, Trail making test Part B.	lower scores on the BDI-II (p=0.001), HADS (p<0.01), and ZBV-trait (p=0.002) showing improvement on these neuropsychological measures. 4. The experimental group reported significantly higher scores for quality of life on the QOLIBRI (p<0.05). 5. On measures of cognitive functioning no significant differences were seen for any outcome measures.
Korman et al. (2018) Israel PCT N=20	**Population:** *Experimental Group (N=10)*: Mean age=30yr; Time post-injury=126.9 days; GCS: 3-12; Mean FIM at admission=53.3. *Control Group (N=10):* Mean age=29.3yr; Time post-injury=118.4 days; GCS: 3-8; Mean FIM at admission=46.8. **Intervention:** Over 2 weeks 5 training sessions took place where the experimental group was trained on a finger to thumb finger sequence task. Neither the TBI control group, nor the healthy control group received any training. All groups were evaluated on this task at two time points. **Outcome Measures:** Number of sequences performed during test time, number of correct sequences performed, performance speed, and number of errors.	*Trained vs Un-trained individuals with TBI* 1. Both groups significantly improved performance speed over the course of testing (p<0.001). With the trained TBI group seeing significantly larger gains (p=0.016). 2. There were no significant changes for either group in the number of errors produced over the testing period. 3. When assessing learning in the TBI group only, significant improvements in speed were seen during the training session (p<0.01). 4. Individual's performance was significantly worse at the end of a session compared to the beginning of a session (p=0.003). *Trained individuals with TBI vs Healthy controls* 5. During pre-training healthy controls completed significantly fewer errors compared to the TBI population (p<0.001). 6. Although both groups improved in performance over training sessions, the healthy control group had significantly greater gains compared to the TBI group (p<0.001). 7. A significant time X group interaction demonstrated that healthy controls had a faster learning trajectory compared to trained individuals with an ABI (p<0.001). 8. Both groups showed a significant decrease in within session gains over the course of testing (p<0.001). 9. No significant differences were seen for between session gains during testing, demonstrating that healthy controls did not significantly out-perform individuals with a TBI who received training.
Bosco et al. (2018) Italy Pre-post	**Population:** *Severe TBI:* Mean age=38.5yr; Gender: Male=16, Female=3; Mean time post-injury=99.4 months; GCS<8.	1. There was a significant difference in scores on the ABaCO between pretreatment and posttreatment scores (p<0.001). There were no

Author Year Country Research Design PEDro Sample Size	Methods	Outcome
N=19	**Intervention:** Groups of 5-6 participants met twice a week for 12 weeks for a total of 24 Cognitive Pragmatic Treatment (CPT) sessions. Participants were assessed at four time points, 3-months pretreatment, immediately before treatment, immediately following treatment, and 3-months post-treatment. **Outcome Measures:** Assessment Battery for Communication (ABaCo), Communications Activities of Daily Living (CADL), Aachener Aphasie test, Attentional Matrices, Trail Making test, Verbal Span, Corsi's Block-Tapping test, immediate and deferred recall test, Tower of London test, Modified Card Sorting test, Raven Colored Progressive Matrices, Sally & Ann, Strange Stories.	significant differences between the two initial time points, or the two posttreatment timepoints. 2. Similar results were seen for the CADL, with individuals showing a significant improvement in their functional communication skills following treatment (p=0.024). 3. Between immediate pretreatment scores and immediate posttreatment scores significant differences were only seen on the Verbal Span (p=0.045), and the Modified Card Sorting test (p=0.004).
Lindelov et al. (2016) Denmark PCT $N_{Initial}$=78 N_{Final}=35	**Population:** *ABI Group (n=17)*: Mean Age=56.1yr; Gender: Male=13, Female=4; Mean Time Post Injury=57d. *Healthy Group (n=18)*: Mean Age=56.1yr; Gender: Male=8, Female=10. **Intervention:** ABI and healthy participants were randomized and analyzed separately. Experimental group participants received 20 sessions of N-back training (N-back), where participants press a key when presented stimulus is identical to the stimulus N back in the sequence. Control group participants received 20 sessions of visual search training (VS), where participants press a key if a target symbol is present in an NxN array of symbols. **Outcome Measure:** Raven's Advanced Progressive Matrices (RAPM), Wechsler Adult Intelligence Scale-IV (WAIS-IV), Working Memory Index (WMI Index, digit span, arithmetic, letter-number sequencing), Operation Span Test (OSPAN), WAIS-IV Processing Speed Index (PSI index, search, coding), Stroop Test.	1. Both ABI and healthy groups showed significant improvement post-intervention on the assigned training tasks (Bayes factor >> 1000). The standardized mean difference was 0.45 for ABI N-back, 6.11 for healthy N-back, 1.06 for ABI VS, and 3.34 for Healthy VS. The healthy group showed greater improvement than the ABI group (Bayes factor >> 1000). 2. No significant differences in improvements between N-back and VS treatments (time x treatment interaction) were found in ABI or healthy groups for WMI-digit span, WMI-arithmetic, WMI-letter-number sequencing, WMI index, PSI-search, PSI-coding, PSI index, RAPM, OSPAN, or Stroop. 3. No significant differences in improvement between healthy and ABI groups (group x time x test interaction) were found for WMI-digit span, WMI-arithmetic, WMI-letter-number sequencing, WMI index, PSI-search, PSI-coding, PSI index, RAPM, OSPAN, or Stroop.
O'Neil-Pirozzi and Hsu (2016) PCT $N_{Initial}$=14 N_{Final}=12	**Population:** TBI=4, CVA=2, Brain tumour=1; Severity: moderate/severe. *Experimental Group (n=7)*: Mean Age=51.3 yr; Gender: Male=5, Female=2; Mean Time Post Injury=20.9 yr; Etiology: TBI=5, CVA=2. *Control Group (n=7):* Mean Age=46.9 yr; Gender: Male=7; Mean Time Post Injury=25.0 yr. **Intervention:** Experimental group participants received BrainHQ, a commercially available online computerized cognitive exercise program (Attention, Brain Speed, Memory, People Skills, Intelligence, and Navigation) for 5 mo, 5 d/wk. Control group participants did not have a private computer and received no intervention.	1. Of the five experimental group participants that completed the study, they completed an average 87% of sessions, initiated an average 25% of sessions, and independently completed an average 7% of sessions. Two participants needed minimum external cues, two participants needed moderate external cures, and one participant needed maximum external cues. 2. Comparing 3 mo prior to intervention with 1 wk prior to intervention, there were no significant differences within either group for WCST, HVLT-R, COWAT, TMT A or B, or SWLS.

Author Year Country Research Design PEDro Sample Size	Methods	Outcome
	Outcome Measures: Number/percentage of sessions completed, Number/percentage of sessions initiated by participants, Number/percentage of sessions completed independently by participants, Mean amount of external cures provided for session completion, Wisconsin Card Sorting Test (WCST), Hopkins Verbal Learning Test-Revised (HVLT-R immediate, delayed), Controlled Oral Word Association Test-FAS (COWAT), Trail Making Test (TMT A and B accuracy and speed), Satisfaction with Life Scale (SWLS), Semi-Structured Interview Questions.	3. There were no significant differences between groups at 1 wk prior to intervention (baseline) for WCST, HVLT-R, COWAT, TMT A or B, or SWLS. 4. Compared to baseline, experimental group showed significant improvement post-intervention for HVLT-immediate (p=0.0255) and SWLS (p=0.0075). There were no significant improvements for WCST, HVLT-delayed, or TMT A or B. 5. Compared to baseline, control group did not show significant differences post-intervention for WCST, HVLT, TMT A or B, or SWL. 6. Compared to control group, experimental group showed significantly higher post-intervention improvements on HVLT-immediate (p=0.0068) and COWAT (p=0.0310). No significant differences between groups were found for changes in WCST, HVLT-delayed, TMT A or B, or SWL. 7. Of the experimental group participants who completed the study, 60% reported improved everyday thinking abilities, 60% reported improved memory, and 20% reported improved attention, organization, and/or problem-solving skills, but 60% reported they would not continue with exercise program post-study completion.
Gabbatore et al. (2015b) Italy Pre-Post $N_{Initial}$=20 N_{Final}=15	**Population:** TBI; Mean Age=36.7 yr; Gender: Male=10, Female=5; Mean Time Post Injury=76.1 mo; Mean GCS=4.5. **Intervention:** Participants completed a cognitive group rehabilitation program focussed on mental representations underlying one's behaviours (2 x/week for 3 months). Each session consisted of comprehension activities (discussing specific communication modalities) and production activities (role-playing activities). Participants were assessed at T0 (3 months before intervention (regular activities during this time), T1 (before intervention), T2 (after intervention) and T3 (3-month follow-up – regular activities during this time). Total study duration was 9 months. **Outcome Measures:** : Assessment Battery for Communication (ABaCo-comprehension, production, linguistic, extralinguistic, paralinguistic, and context), Verbal Span Task (VST), Spatial Span Task (SST), Attentive Matrices Test (AMT), Trail Making Test (TMT), Tower of London Test (TOL), Colored Progressive Matrices Raven (CPM Raven),	1. No significant improvements in ABaCo (production and comprehension) were observed from T0 to T1. 2. Participants showed significant improvements from T1 to T2 for ABaCo comprehension (p<0.001), production (p<0.001), linguistic (p=0.005), extralinguistic (p=0.008), paralinguistic (p=0.020), and context (p=0.010). 3. The improvements made during the treatment period were stable between T2 and T3 for both Comprehension (p=0.860) and Production (p=0.320). At T3, AbaCo scores did not show significant differences from T2. 4. There was no significant difference between T1 and T2 on the VST (p=0.490), SST (p=0.740), AMT (p=0.350), TMT (p=0.450), TOL (p=0.500), CPM Raven (p=0.090), AAT (p=0.220), Sally-Ann (p=0.580), or strange stories task (p=1.000). 5. There was a significant improvement between T1 and T2 on the IDR (p=0.010) and WCST (p=0.003).

Author Year Country Research Design PEDro Sample Size	Methods	Outcome
	Aachener Aphasie Test-Denomination Scale (AAT), Sally-Ann Task, Strange Stories Task, Immediate and Deferred Recall Test (IDR), Wisconsin Card Sorting Test (WCST).	
Hellgren et al. (2015) Sweden Case Series N=48	**Population:** Cerebral infarction=23%, TBI=21%, Infection=19%, Intracerebral hemorrhage=13%, Subarachnoid hemorrhage=10%, Brain tumor=8%, Other=6%; Mean Age=43.7 yr; Gender: Male=30, Female=18; Mean Time Post Injury=51.2 mo. **Treatment:** Participants received a working memory training program (Cogmed) consisting of various visuospatial and verbal working memory tasks. There were 4-5 sessions/wk for 5-7 wk, consisting of 45-60 min of intense exercise with one break. Occupational therapist coaches were present during every session and provided weekly feedback in addition to continuous feedback from the computer program. **Outcome Measure:** Paced Auditory Serial Attention Test (PASAT 2.4), Forward and Backward Block Repetition, Listening Span Task, Canadian Occupational Performance Measure (COPM performance and satisfaction), EuroQol descriptive (EQ-5D Index), EuroQol Visual Analogue Scale (EQ-VAS), Working Memory Index (WM Index).	1. At 20 wk post-training, there were significant improvements in PASAT ($p<0.001$), Listening Span ($p<0.001$), Forward block repetition ($p<0.001$), Backward block repetition ($p<0.001$), COPM performance ($p<0.001$), COPM satisfaction ($p<0.001$), EQ-5D index ($p=0.009$), and EQ-VAS ($p<0.001$) compared to baseline. 2. Compared to baseline, all participants significantly improved their WM Index at 20 wk follow-up ($p<0.001$). 3. No significant differences in treatment effect were found for all outcomes in terms of sex or time post-injury, except for ≤18 mo since injury exhibiting more improvement than >18 mo in terms of WM index difference ($p<0.050$), COPM performance improvement ($p<0.050$), and COPM satisfaction improvement ($p<0.050$).
Li et al. (2015) USA Pre-Post $N_{Initial}$=13 N_{Final}=12	**Population:** Stroke=5, TBI=5, Brain tumor=2; Mean Age=61 yr; Gender: Male=10, Female=2. **Intervention:** Participants received the computer-based cognitive retraining program, Parrot Software. The following eight modules were each completed in separate 1 h sessions: Visual Instructions, Attention Perception and Discrimination, Concentration, and Visual Attention Training, Remembering Written Directions, Remembering Visual Patterns, Remembering Written Letters, and Remembering Written Numbers. **Outcome Measures:** Montreal Cognitive Assessment (MoCA overall, attention, memory), Medication-box Sorting Task.	1. Compared to baseline, there was a significant mean increase in overall MoCA of 3.25 ($p=0.030$) post-intervention. However, the attention and memory subscales did not show significant differences. 2. There were no significant differences before and after intervention for the medication-box sorting task. 3. Participants with previous computer-based cognitive retraining experience had significantly more MoCA improvement than those without ($p<0.010$). 4. Age, education level, or type of ABI diagnosis did not have any significant effects on MoCA or medication-box scores.
Li et al. (2013) USA Pre-Post N=11	**Population:** ABI; Mean Age=49.45 yr; Mean Time Post Injury=21.27 yr. **Intervention:** All participants completed eight 60-minute sessions using the attention and memory sub programs of the computer-based cognitive retraining Parrot Software. The participants focused on one of the eight subprograms during each session with each subprogram containing 10 lessons with	1. There was a significant improvement in attention cognitive assessment scores from pre to post intervention (mean change=2.091; $p<0.005$). 2. There was a significant improvement in memory cognitive assessment score from pre to post intervention (mean change=1.73; $p<0.050$).

Author Year Country Research Design PEDro Sample Size	Methods	Outcome
	increasing difficulty. Assessments were conducted before and after intervention. **Outcome Measure:** The Cognitive Assessment (Attention & Memory).	
Johansson & Tornmalm (2012) Sweden Pre-Post N=18	**Population:** TBI=5, Brain Tumor=6, Stroke=7; Mean Age=47.5yr; Gender: Male=13, Female=5; Mean Time Post Injury=7yr. **Intervention:** All participants received a working memory training program (WMTP) using computerized training software (Cogmed QM), coaching, education and peer support. This consisted of visual and auditory working memory tasks. Training ranged from 20-25 sessions. **Outcome Measures:** Cognitive Failures Questionnaire (CFQ), Canadian Occupational Performance Measure (COPM), CogMed QM tasks.	1. A significant reduction in cognitive problems was found through self-rating on the CFQ (median change 5, p=0.018). 2. A significant improvement on self-rating scores on the COPM were found for performance (median change=1.4, p=0.008) and satisfaction with performance (median change=1.8, p=0.010). 3. Significant improvements were noted on Cogned QM tasks (p<0.001).
Raskin et al. (Raskin et al., 2012) United States PCT N=18	**Population:** *Brain injury (N=8):* Mean age=41.75yr; Gender: Male=4, Female=4; Mean GCS=8.5; Mean time post-injury=84.22mo. *Healthy Adult (N=10):* Mean age=45yr; Gender: Male=2, Female=8. **Intervention:** Participants with a brain injury were given a memory intervention which included behavioral interventions, metacognitive strategies, and restorative approaches and compared to healthy controls. **Outcomes:** Assessment of Intentional Memory (AIM), Community Integration Questionnaire (CIQ), Prospective Memory Questionnaire (PMQ), Everyday Memory Questionnaire (EMQ), Diary Study.	1. All participants increased the time between recall on the ProM tasks. 2. Both groups improved scoring on the AIM with the 2-min time delay assessment, but the BI group had lower scores when the delay was pushed to 15 mins. 3. Individuals in the brain injury group showed significant improvement in total AIM scores (p<0.05), and a significant reduction in the number of errors made (p<0.05). 4. There were no significant improvements on the CIQ, or PMQ. 5. The BI group had a significant decrease in EMQ scores (p<0.05). And a significant increase in memory scores related to the Diary Study (p<0.05).
Serino et al. (2007) Italy Case Series N=9	**Population:** TBI: Age range=16-57 yr; Gender: male=6, female=3; Time since injury=6-78 months. **Intervention:** A long sequence of numbers was presented, and patients were asked to add each new number to the number preceding it and say the sum out loud. Two additional tests (the Months tasks and the Word tasks) were also administered in a similar way. The GST and the WMT were each 4 sessions/week, for 4 weeks. To vary tasks and their level of difficulty, in the interstimulus interval was varied. **Outcome Measure:** Working memory training (WMT), Paced Auditory Serial Addition Test (PASAT), Months task	1. Study results indicate the greatest improvement in performance occurred from the intermediate to the final sessions (p<0.0005) after the WMT. 2. Improvement from the initial to intermediate sessions did not show any significant improvement in working memory (p<0.460) after GST. 3. Working memory (p<0.050), divided attention (p<0.050), executive function (p<0.050), and long-term memory (p<0.050) for subjects were significantly improved in the final session compared to the intermediate session. 4. The same was not noted on the speed processing and sustained attention tasks (p>0.050). Working memory training tasks were also found to improve scores on various psychosocial outcomes.

Author Year Country Research Design PEDro Sample Size	Methods	Outcome
Hewitt et al. (2006) (Hewitt et al., 2006) United Kingdom PCT N=30	**Population:** *Control Group (N=15):* Mean age=33.13yr; Gender: Male=10, Female=5; Mean time post-injury=7yr. *Experimental Group (N=15):* Mean age=38.47yr; Gender: Male=10, Female=5; Mean time post-injury=5.3yr. **Intervention:** Both groups completed sessions where they were asked to describe procedures for completing everyday tasks. The experimental group underwent additional procedural training which included memory retrieval prompts. **Outcomes:** Effectiveness of memory plan, number of steps remembered in procedures, number of specific memories, Rivermead Behavioral Memory Test (RBMT).	1. There was a significant between groups difference post-intervention for the effectiveness of memory strategies with the experimental group showing improved scores ($p<0.01$). 2. The experimental group were able to communicate significantly more steps on procedures post-intervention compared to the control group ($p<0.03$). 3. There was a significant within-subjects effect for the number of specific memories recalled post-intervention compared to pre-intervention ($p<0.01$). 4. There were significant correlations between the number of specific memories produced and the effectiveness of the plan ($p<0.01$), and the number of steps ($p<0.01$). 5. RBMT scores were significantly associated with the difference in the number of specific memories between pre and post-intervention ($p<0.02$), but not for effectiveness of plan used, of the number of relevant steps in the procedure.
Tam & Man (2004) China PCT N=32	**Population:** TBI. *Self-Pace Group (n=6)*: Mean Age=40.5yr; Gender: Male=4, Female=2. *Feedback Group (n=6)*: Mean Age=33.3yr; Gender: Male=4, Female=2. *Personalized Group (n=6)*: Mean Age=32.6yr; Gender: Male=3, Female=3. *Visual Representation Group (n=6)*: Mean Age=39.8yr; Gender: Male=3, Female=3. *Control Group (n=8)*: Mean Age=45yr; Gender: Male=4, Female=4. **Treatment:** Patients were randomly assigned into one of four parallel computer-assisted retraining groups: 1) self-paced, 2) feedback (i.e., immediate feedback), 3) personalized (in actual living environment), or 4) visual presentation (colourful, bright and attractive presentation). There was a total of 10 sessions, each lasting 20-30min. The control received no computerized retraining. **Outcome Measure:** Rivermead Behavioural Memory Test (RBMT).	1. After intervention, all groups receiving the computer-assisted memory programs performed significantly better in memorizing and remembering 'drilled content' ($p<0.05$). 2. No significant differences were found between pre- and post-RBMT scores in any of the treatment groups. 3. All memory-training conditions showed a positive trend in the treatment group as compared to the control group although there were no statistical differences between measures.
Boman et al. (2004) Sweden Pre-Post N=10	**Population:** TBI: Mean age=47.5 yr; Gender: male=5, female=5; Time Post injury=9-40 months. **Intervention:** Each person participated in an individual cognitive training session for 1 hr/3x a week for 3 weeks at home or work. The program included attention process training (APT), generalization for training and teaching of compensatory strategies for self-selected	1. For the following: sustained attention, selective attention and alternating attention significant changes ($p<0.050$, $P<0.050$, $p<0.010$ respectively) were noted in the scores of the APT test and Digit Span task between the pre to post training session and the 3 month follow up. 2. Score increases ($p<0.050$) on the RMBT were found at the 3-month follow up compared to

Author Year Country Research Design PEDro Sample Size	Methods	Outcome
	cognitive problems. Identification of cognitive problems in everyday life was also part of the compensatory strategy. **Outcome Measures:** Digit Span Test, Claeson-Dahl test, Rivermead Behavioural Memory test (RBMT), Assessment of Motor and Process Skills, European Brain Injury Questionnaire.	the RMBT scores at the pretest. 3. When looking at changes in the RBMT score pre to post training, changes were not found. 4. No significant changes were found (pre to post and pre to 3-month follow up) when looking at the scores on the Claeson-Dahl Memory
Quemada et al. (2003) Spain Pre-Post N=12	**Population:** Mean Age: 33.1 yr; Gender: male=6, female=6; GCS Score=5.7; Condition: TBI. **Intervention:** Individualized treatment using Wilson's Structured Behavioral Memory Program in 50-minute sessions daily for 6 months. **Outcome Measures:** Rey-Osterrieth Complex Figure Test (REY), California Verbal Learning Test (CVLT), Rivermead Behavioural Memory Test (RBMT), Memory Failures in Everyday Memory Questionnaire (MFE) Tests.	1. All patients achieved meaningful functional gains. 2. Improvements were not found using REY, RBMT or MFE measures. 3. There were modest improvements in some scales of the CVIL (p=0.030, p=0.090, p=0.050).
Laatsch et al. (1999) USA Case series N=5	**Population:** TBI; Age=18-65 yr; Time Post-Injury=2-48 months; **Intervention:** Cognitive rehabilitation therapy (CRT) programme in a longitudinal protocol involving a resting SPECT and neuropsychological evaluation are pre-treatment, post-treatment and post non-treatment intervals. **Outcome Measures:** Neuropsychological Measures.	1. NP measures: WAIS-R, WMS-R, CVLT, RCFT, SCWT, WCST or ACT, SPECT image. 2. SPECT data revealed significant increases in cerebral blood flow during the treatment period (p<0.050). 3. CRT was found to be effective in improving both NP and everyday functioning. All patients were able to be more productive in their lives following treatment.
Parente et al. (1999) USA Pre-Post N=72	**Population:** TBI: Mean Age=32 yr; Gender: Male=39, Female=33; Injury Etiology: Motor Vehicle Accident=46, Other=26. **Intervention:** Participants were given tasks that trained working memory for 1 hour between pre- and post-test measurement. Control clients matched to treatment group by sex and chronicity. **Outcome Measures:** Digit Span Task; Letter/Number Sequencing Tasks from WAIS-III.	1. No significant differences between Digit Span test. WAIS-III differed significantly pre/post treatment (p<0.050).
Chen et al. (1997) USA Case-Control N=40	**Population:** Age=18+years; Gender: Male=27, Female=13; Condition: TBI. **Intervention:** Divided retrospectively into computer-assisted rehabilitation (CACR) and traditional therapy groups **Outcome Measures:** Neurophysiological Test Scores (WAIS-R; WMS).	1. Both groups made significant post-treatment gains on the neurophysiological test scores (p<0.050), with the CACR group making significant gains on 15 measures (p<0.050) and the comparison group making significant gains on seven measures (p<0.005). 2. However, no significant difference was found between groups on their post-treatment gains.
Jennet & Lincoln (1991) (Jennett & Lincoln, 1991) United Kingdom PCT	**Population:** Mean age=52.3yr; Gender: Male=11, Female=8; Mean time post-injury 2-111mo. **Intervention:** Individuals were randomly assigned to participate in a memory strategy	1. There were no significant differences on the RBMT, or the SMQ. 2. There was no significant difference in the number of items individuals reported being bothered by, however the intensity to which

Author Year Country Research Design PEDro Sample Size	Methods	Outcome
N=18	program in a group setting or be put on a waitlist. **Outcomes:** Rivermead Behavioral Memory Test (RBMT), Subjective Memory Questionnaire (SMQ), number and intensity of memory problems bothering individuals, use of memory aids.	they were bothered by them significantly decreased (p=0.03). 3. There was a significant decrease in the number of memory aids used by the experimental group (p<0.05).

PEDro = Physiotherapy Evidence Database rating scale score (Moseley et al., 2002a)

Discussion

Similar to internal memory strategies, many potential interventions have been studied, with little overlap between studies themselves in terms of methodology. A variety of trademarked cognitive programs have been evaluated in an attempt to improve learning and memory following an ABI. Constantinidou et al. (2008) evaluated the Categorization Program for 13 weeks in an RCT, and found that although individuals who received the program performed better on measures of executive function, there were no significant improvements seen in learning or memory. Chiaravalloti et al. (2016) compared the efficacy of the modified Short Memory Technique to conventional therapy for the improvement of memory post TBI. Amongst the memory assessments quantified, significant improvements were seen only in two specific categories; the Memory Assessment Scale- Prose Memory (MAS-PM) and “hidden belonging task” of the Rivermead Behavioural Memory Test (RBMT). A follow-up study further recognized the lack of improvement in the treatment group compared to controls in terms of memory capacity; however, they did note that working memory capacity and long-term memory retainment were positively correlated with each other (Sandry et al., 2016). In a prospective cohort study, Johansson and Tornmalm (2012) examined the benefits of Cogmed QM (computerized training software) coaching, education and peer support to help improve the daily functioning of participants. Results show the Cogmed QM program helped to improve working memory and these benefits were seen at the 6-month follow up. RehaCom software has also been evaluated in a single study (Fernández et al., 2012). Individuals significantly improved on the Wechler Memory Scale for overall memory and also on measures of attention (Fernández et al., 2012). Recently, BrainHQ, a commercially available online computerized cognitive exercise program, did not significantly improve attention outcomes over time or compared to no intervention (O'Neil-Pirozzi & Hsu, 2016). Gabbatore et al. (2015) implemented a cognitive group rehabilitation program for patients post TBI, and discovered that compared to before the intervention, patient’s recall (IDR), attention (WCST), and communication skills (ABaCo) all significantly improved. Parrot Software is another computer-based cognitive retraining program, and was investigated by a pre-post study assessing the efficacy of using eight modules focussed on attention and memory (Li et al., 2015; Li et al., 2013).

While significant post-treatment improvements in attention and memory on the Cognistat assessment were found in a pilot study (Li et al., 2013), a subsequent study did not find significant improvements on the attention and memory subscales of the Montreal Cognitive Assessment (MoCA) or a medication-box sorting task despite significantly improved overall MoCA scores (Li et al., 2015). However, in one RCT Dou et al. (2006) demonstrated that computer assisted memory training may not be superior to therapist administered memory training as both groups improved on measures of memory over time compared to a no-treatment control group, but did not significantly differ from each other. Finally, Chen et al. (1997)

studied the effect of computer assisted cognitive rehabilitation versus traditional therapy methods. While measures of attention significantly improved in both groups after treatment, no significant differences were observed between groups (Chen et al., 1997). Cumulatively, by observing studies from across a period of nearly 20 years, the literature reveals little support for the use of computer software programs for the improvement of executive function post TBI. It should be noted no specific software program was evaluated in more than one study; ,therefore limited conclusions can be made on their efficacy compared to therapist administered therapy or to each other. However, cognitive-based computer programs have generally been shown to be effective on measures of cognitive functioning (Johansson 2012).

Several specific non-computerized learning and memory interventions have also been evaluated in singular studies. In an RCT conducted by Vas et al. (2011), 28 individuals who had sustained a TBI and were at least 2 years post injury, were assigned to one of two groups: the strategic memory and reasoning training group or the Brain Health Workshop group. Each group received 15 hours of training over an eight-week period. Those in the strategic memory and reasoning training group were given information about brain injuries, were asked to read pieces of literature on brain injury and were given homework assignments to be completed for the next meeting. The strategic memory and reasoning training sessions were built around three strategies: strategic attention, integration (*combining important facts to form higher order abstracted meaning*) and innovation (*derive multiple abstract interpretations*). Those in the brain health workshop group participated in information sessions. Sessions for the brain health workshop groups included an introduction to brain anatomy, functions of the brain, neuroplasticity, and the effects of lifestyle on the brain (diets, exercises and cognitive changes following a TBI). Study results indicate that those assigned to the strategic memory and reasoning training group showed significant improvement on gist reasoning and measures of executive function.

With respect to attention process training, it was shown that individuals receiving attention remediation significantly improved in memory and attention measurements compared to controls who had education alone (Sohlberg et al., 2000). Conversely, two trials did not find significant differences between groups for attentional, functional, and/or cognitive skills assessed (Lindelov et al., 2016; Novack et al., 1996). Novack et al. (1996) compared focused hierarchical attentional learning with an unstructured non-sequential, non-hierarchical intervention, while Lindelov et al. (2016) compared N-back training with visual search training. Two older RCTs have evaluated attention training programs directly to memory training programs with limited results. An RCT from 1990 evaluated a non-specified memory training program and compared it directly to an attention training program and found that neither program actually improved measures of memory (Niemann et al., 1990). However, the attention training program did improve some measures of attention, but this was not consistent across all measures of attention evaluated (Niemann et al., 1990). Ryan & Ruff (1988) found similar results where neither the applied memory training program nor the attentional program significantly improved measures of memory or learning in individuals. Overall there is weak evidence in support of training programs as an effective rehabilitation intervention for attention.

In another RCT, 45 individuals were randomly assigned into one of four treatment groups (Shum et al., 2011). The treatment groups consisted of four different intervention programs: self-awareness plus compensatory prospective memory training; self-awareness training plus active control; active control plus compensatory prospective memory training and active control only. Pre-intervention scores on the CAMPROMPT did not reveal any significant differences between any of the groups. Those assigned to the compensatory prospective memory training groups showed greater changes in strategies used to improve memory. Compensatory prospective memory training included use of a diary or organizational devices, and group members were encouraged to use written reminders, appointments and note taking. Although at total of 45 participants started the study, only 36 finished. Further support for emotional oriented intervention can be found in an earlier study by Rath et al. (2003). The group completed an RCT comparing two cognitive rehabilitation therapies: conventional (cognitive remediation and psychosocial components) versus an innovative rehabilitation approach focusing on emotional self-regulation and clear thinking. Outcomes were measured across multiple domains of cognition including attention, memory, reasoning, psychosocial functioning, and problem-solving measures. Significant changes comparing baseline to post intervention outcomes were seen for each group, however, the improvements were different for the interventions. No between-group comparisons were made.

The effects of hypnosis, as delivered in a targeted or non targeted manner, on memory, attention, and cognitive function in a mixed TBI and stroke population has been studied (Lindelov et al. 2017). The researchers showed that working memory, attention, and cognitive function could be transiently increased during targeted hypnosis, however the benefits of the treatment were not sustained when the treatment was discontinued. This last finding calls into question the practicality of the intervention, as it may not be feasible to deliver targeted hypnosis to patients post brain injury on a continual basis. Another unique intervention aimed at improving memory following an ABI was an RCT evaluating meatball making (Eakman & Nelson, 2001). Individuals received either hands-on or verbal instructions for making meatballs and were required to reproduce the meatballs at a later time. In this instance meatballs were used as an example to explore the benefits of modelling compared to verbal instruction only on memory consolidation. It was found that the hands-on meatball making group remembered significantly more steps in the making process compared to the verbal instruction only group (Eakman & Nelson, 2001) suggesting that modelling may be more effective than verbal instruction alone. Another study which compared the type of instruction given showed that asking individuals to describe procedures in detail and providing retrieval prompts was significantly more beneficial for recall than individuals training by describing procedures alone (Hewitt et al., 2006). These studies support the use of a combination of modelling and instructional techniques to improve memory.

Thickpenny-Davis and Barker-Collo (2007) randomly assigned 14 individuals to either the treatment or control group. Those in the treatment group participated in a memory rehabilitation program. The memory groups consisted of eight learning modules each 60 minutes long. They ran twice a week for 4 weeks. Memory improvement and difficulties were evaluated. Overall a reduction in memory impairment was noted at the end of the 4 weeks of intervention and again at the 1-month follow-up time period. Hellgren et al. (2015), found that a memory training program was successful in improving attentional scores on the Paced-Auditory Serial Attention Test, as well as further enhancing memory in general which is discussed later on in the chapter. Quemada et al. (2003) examined memory rehabilitation following severe TBI in 12 individuals (no controls). The program ran for 6 months (50-minute sessions 5 days a week for 5 months and then 3 days a week for one month) and followed a specified format utilizing behavioural compensation techniques, mnemonic strategies, and environmental adaptations, external and internal aides. Results indicated little improvement in standard measures of memory functioning, although patients and family members report meaningful functional gains (self-report and observed behaviour in everyday functioning).

Only one study (Serino et al., 2007) described a specific task that was successful in improving memory. This cognitive task involved mental addition in combination with two other standardized tasks and was an effective strategy for improving working memory. Boman et al. (2004) in a study of ten individuals with mild or moderate TBI, after completing 1 hour of an individual cognitive training three times a week for 3 weeks, significant improvement was noted on the Rivermead Behavioural Memory Test at 3-month follow-up compared to pre-test scores. Changes on the Claeson-Dahl Memory test did not increase pre to post to 3-month follow-up. The findings of the previous study support the findings of the study by Laatsch et al. (1999) where cognitive rehabilitation therapy was found to increase productivity and everyday functioning. This older study also had the benefit of reporting SPECT imaging results, which revealed increases in cerebral blood flow during the intervention. Similar findings were reported in an RCT by Novakovic-Agopian et al. (2011), which examined the effects of goals training and education in an RCT crossover study. While education was shown to minimally improve memory, specific goals training significantly improved working memory, mental flexibility, learning and delayed recall (Novakovic-Agopian et al., 2011). A Cognitive Pragmatic Treatment program was evaluated over the course of 24 sessions with participants being assessed at four different time points (Bosco et al., 2018a). The results showed strong effects on communication and activities of daily living, with verbal span only improving immediately following treatment but differences were not maintained at follow-up (Bosco et al., 2018a).

Specific interventions which were not shown to have positive effects on memory include time pressure management (Fasotti et al., 2000), individual versus group therapy (Leśniak et al., 2018), finger sequencing tasks (Korman et al., 2018), and the Intensive Neurorehabilitation Programme (Holleman et al., 2018b). Lesnaik et al. (2018), compared the effects of individual versus group therapy on memory and found that although both groups improved over time, there were no significant differences between groups. Similar to the previous study, time pressure management was not shown to significantly improve memory outcomes compared to control (Fasotti et al., 2000). With finger sequencing tasks, individuals who were trained versus untrained on the task showed no significant differences in the number of errors made, however the trained group saw a significant increase in performance speed compared to the control group (Korman et al., 2018). In a recent prospective controlled trial, a formal protocol for the Intensive Neurorehabilitation Programme showed no significant effects on the Rivermead Behavioral Memory Test, however depression and anxiety were seen to be significantly reduced (Holleman et al., 2018a).

General components of effective programs have been shown to be behavioral interventions, metacognitive strategies, and restorative approaches which tackle multiple areas of functioning and processes (Raskin et al., 2009). One study demonstrated that a memory program which included all of these components elevated memory scores in individuals with an ABI similar to that of healthy controls (Raskin 2009). A small 1991 RCT also provides support that memory programs which include memory strategies can also significantly decrease dependence on memory aids for those with an ABI {Jennett, 1991 #243}

Conclusions

There is level 1b evidence that hypnosis compared to no treatment may not be effective at improving memory in individuals post ABI.

There is level 1b evidence that individual memory therapy is no more effective than group memory therapy for those with an ABI.

There is level 2 evidence that programs involving multiple learning strategies (such as modelling, reciting, verbal instruction, and observation) are more effective than singular strategies for those with an ABI.

There is level 1b evidence that the Short Memory Technique may not be more effective than standard memory therapy at improving memory in individuals post ABI.

There is level 1b evidence that the Categorization Program, and Strategic Memory and Reasoning Training (SMART) may be effective for improving memory compared to standard therapy in individuals with an ABI.

There is level 2 evidence that time pressure management training is no more effective than concentration training at improving memory for those with an ABI.

There is level 2 evidence that N-back training compared to virtual search training is not effective for improving memory in those with an ABI.

There is level 4 evidence that Cognitive Pragmatic Treatment, Cogmed QM, and RehaCom software may improve memory and cognitive function in those with an ABI.

There is level 2 evidence that participation in a goals training program, followed by an educational program, may be more effective for improving memory in post ABI individualscompared to receiving the treatment conditions in reverse order.

There is level 2 evidence that finger sequence training, compared to no training, may not be effective for improving memory following an ABI.

There is level 1b evidence that compensatory memory strategies, self-awareness training, and participation in memory group sessions may be effective for improving memory in post ABI individualscompared to no treatment.

There is level 2 evidence that general memory rehabilitation programs are effective, compared to standard therapy, at improving memory for those with an ABI.

There is level 2 evidence that the Intensive Neurorehabilitation Programme is not effective for improving memory compared to controls in those with an ABI.

There is level 2 evidence that both computer-administered and therapist-administered memory training may be more effective than no treatment for improving memory in ABI participants. However, no treatment appears to be better than the other.

There is level 2 evidence that both cognitive remediation and emotional self-regulation may be effective at improving different elements of memory in individuals post ABI.

There is level 2 evidence that non-specific computer-based memory retraining compared, self-paced or otherwise, may not be effective at improving memory in those with an ABI.

There is conflicting level 1b evidence as to whether or not attention training programs may be effective for improving memory compared to no therapy, but positive level 1b evidence that it is not more effective than memory training programs.

There is level 2 evidence that BrainHQ is not an effective program for improving memory and learning compared to no intervention in individuals post ABI.

There is level 4 evidence that using mental representations and role-playing may not be effective at improving memory in individuals post ABI.

There is level 4 evidence that Cogmed training software may improve working memory performance and occupational performance in individuals post ABI.

There is conflicting (level 4) evidence regarding whether or not Parrot software is effective at improving memory and learning in individuals post ABI.

There is level 4 evidence that mental addition tasks may improve working memory in individuals post ABI.

There is level 4 evidence that the Wilson's Structured Behavioral Memory Program is not effective for improving memory post ABI.

Memory-retraining programs appear effective, particularly for functional recovery although performance on specific tests of memory may or may not change.

Some specific computer-based softwares seem to be effective for improving memory post ABI.

Computer-based interventions may be as effective as therapist administered interventions.

Emotional self-regulation therapy may be effective for improving specific elements of memory.

Attention training programs may not be effective for improving memory, but memory training programs are.

Interventions which include multiple learning techniques such as modelling, observation, verbal instruction, etc. are more effective than interventions which include a singular learning method.

6.2.1.3 Cranial Electrotherapy Stimulation

Cranial electrotherapy stimulation (CES) is the application of less than 1 mA of electric current to the cranium. This intervention has been used to treat a variety of disorders, including withdrawal of patients with substance abuse (Michals et al., 1993). The effect of CES for the improvement of memory following brain injury was investigated.

Table 6.19 The Effect of Cranial Electrotherapy Simulation on Memory Post ABI

Author Year Country Research Design PEDro Sample Size	Methods	Outcome
Lesniak et al. (2014) Poland RCT PEDro=8	**Population:** Severe TBI=23; Mean Age=28.7yr; Gender: Males=17, Females=6; Mean Time Post Injury=18.1mo.	1. No significant differences between groups post treatment were found on any measures except a moderate

N=23	**Intervention:** Participants were randomized to the Treatment Group: transcranial direct current stimulation (tDCS), or the Control Group with sham therapy. Assessments were done at admission, immediately before treatment, after 3wk rehabilitation, and 4mo after completion. **Outcome Measure:** Cambridge Neuropsychological Test Automated Battery (CANTAB), Rey's Auditory Verbal Learning Test (RAVLT), Patter Recognition Memory test (PRM), Paced Auditory Serial Addition Test (PASAT), Spatial Span Test (SSP), Rapid Visual Information Processing (RVP), European Brain Injury Questionnaire (EBIQ).	improvement in the treatment group on the RVP (p=0.007). 2. At the 4mo follow-up there were no significant differences between groups.
Michals et al. (1993) USA RCT PEDro=7 N=22	**Population:** Mean Age: 24.8 yr; Gender: male=17, female=5; Mean Time Post-Injury: 4.2 yr; Condition: TBI. **Intervention:** A double blind, sham controlled trial on the effectiveness of cranial electrotherapy stimulation (CES) evaluating short-term memory and cognitive functions in TBI patients. **Outcome Measure** Wechsler Memory Scale-Revised; California Verbal Learning Test, Recurring Figures Test.	1. Results revealed that CES stimulation in brain-injured patients did not improve memory or immediate and delayed recall compared with controls. 2. Repeated trial effects showed significant increase in both intervention and control group, however there was no significant differences between groups.

PEDro = Physiotherapy Evidence Database rating scale score (Moseley et al., 2002a).

Discussion

Michals et al. (1993) studied cranial electrotherapy stimulation and its effect on post-traumatic memory impairment in clinical care patients with a closed head injury. Patients received CES or sham CES treatments for 40 minutes daily over a period of four weeks. The group receiving CES treatment did not improve in their memory performance, nor did their immediate or delayed recall improve. Further, with retesting, both the CES and the sham CES group showed a similarly significant trend with no group performing any better than the other. These results suggest that CES stimulation in brain-injured patients does not improve memory functioning.

Conclusions

There is level 1b evidence that cranial electrotherapy stimulation may not improve memory and recall compared to sham stimulation post TBI.

Cranial electrotherapy stimulation may not be effective at enhancing memory and recall abilities following TBI.

6.2.2 Pharmacological Interventions

6.2.2.1 Donepezil

The effectiveness of Donepezil, a cholinesterase inhibitor, in improving cognitive and memory functions following brain injury has been assessed. Cognitive impairments negatively impact patient autonomy, affecting one's ability to return to work or school, and live alone (Masanic et al., 2001). When tested in individuals diagnosed with Alzheimer's disease, Donepezil has been found to be useful in treating memory problems (Morey et al., 2003; Walker et al., 2004). Donepezil's impact on cognitive function and memory in a TBI population is explored in the table below.

Table 6.20 The Effect of Donepezil on Memory and Cognitive Functioning Post ABI

Author Year Country Research Design PEDro Sample Size	Methods	Outcome
Zhang et al. (2004) USA RCT PEDro=7 N=18	**Population:** TBI; *Group A (n=9)*: Mean Age=33 yr; Gender: Male=6, Female=3; Mean GCS=9.3; Mean Time Post Injury=4.6 mo; *Group B (n=9)*: Mean Age=31 yr; Gender: Male=7, Female=2; Mean GCS=8.9; Mean Time Post Injury=3.9 mo. **Intervention:** In a randomized crossover trial, Group A received oral donepezil for the first 10 wk, followed by a washout period of 4 wk. At the conclusion of the washout period, patients received a placebo for 10 wk. Group B received the treatments in the opposite order. Donepezil was administered at 5 mg/d for the first 2 wk, and at 10 mg/d for the remaining 8 wk. **Outcome Measures:** Auditory (AII) and Visual (VII) subtests of Wechsler Memory Scale-III, Paced Auditory Serial Addition Test (PASAT).	1. At week 10, Group A achieved significantly better scores in AII (95.4±4.5 versus 73.6±4.5; p=0.002), VII (93.5±3.0 versus 64.9±3.0; p<0.001), and in the PASAT (p≤0.001) compared to Group B. 2. This increase in scores in Group A were sustained after washout and placebo treatment (week 24), leading to no significant differences in AII (105.9±4.5 versus 102.4±4.5; p=0.588), VII (91.3±3.0 versus 94.9±3.0; p=0.397), and PASAT (p>0.100) compared to Group B at study end. 3. Within-group comparisons showed that patients in both Group A and Group B improved significantly in AII and VII (p<0.050), as well as in PASAT (p<0.001), after receiving donepezil.
Khateb et al. (2005) Switzerland Pre-Post $N_{initial}$=15 N_{final}=10	**Population:** TBI; Mean age=43 yr; Gender: Male=8, Female=7; Mean Time Post Injury=42 mo. **Intervention:** Patients were administered donepezil 5 mg/day for 1mo, followed by 10 mg/day for 2 mos. **Outcome Measures:** Stroop test, Trail Making Test (TMT), Rey Auditory Verbal Memory Test (RAVMT), Test for Attentional Performance (TAP).	1. 4 of 15 participants stopped due to side effects within the first week (e.g., nausea, sleep disorders, anxiety, dizziness, etc.). 2. Changes on the neuropsychological evaluation show modest improvement, the comparison of the global score of all questionnaires before and after therapy was marginally significant (p=0.058). 3. A significant improvement in executive function was only found for the Stroop Colour naming test (87.3±22.9 to 79.5±19.1, p=0.030); for learning and memory the RAVMT-learning (47.7±6.9 to 53.5±5.0, p=0.050); and for attention, the errors subsection of divided attention (5.8±3.3 to 2.9±2.7, p=0.030).
Morey et al. (2003) USA Case Series N=7	**Population:** TBI; Mean Age=30.7 yr; Gender: Male=5, Female=2; Mean Time Post Injury=33.3 mo. **Intervention:** Following baseline cognitive testing (T1), each participant began a 6mo treatment phase with 5 mg/d donepezil for the first 4 wk, then with 10 mg/d for the final 5 mo (T2). Washout period then occurred for 6 wk (T3). Another 6-mo treatment period took place with participants receiving 5 mg/d donepezil for the entire period (T4). **Outcome Measures:** Brief Visual Memory Test-Revised (BVMT-R), Hopkins Verbal Learning Test, digit span and letter-number sequence subtests of	1. Significant improvements (p<0.050) from T1 to T2 were observed for the following: Trial 1 of the BVMT-R, Trial 3 of the BVMT-R, total score of the BVMT-R, and delayed recall trial of the BVMT-R. No significant differences were identified for other measures, or across other testing intervals.

Author Year Country Research Design PEDro Sample Size	Methods	Outcome
	Wechsler Adult Intelligence Scale-Revised III, Controlled Oral Word Association Test, Memory Functioning Questionnaires.	
Masanic et al. (2001) Canada Pre-Post N=4	**Population:** TBI; Age Range=24-35 yr; Gender: Male=4, Female=0; GCS Range=3-8; Time Post Injury Range=35-46 mo. **Intervention:** Participants received 5mg donepezil daily for 8 wk, followed by 10mg daily for 4 wk. Washout period then occurred for 4 wk. Assessments occurred at baseline, and at weeks 4, 8, 12, and 16. **Outcome Measures:** Rey Auditory Verbal Learning Test (RAVLT), Complex Figure Test (CFT), Rivermead Behavioural Memory Test (RBMT).	1. Mean scores for short-term and long-term recall on the RAVLT improved by 1.03 (1.25±1.89 at baseline to 3.00±2.70 at week 12) and 0.83 (0.50±0.58 at baseline to 2.50±2.38 at week 12) standard deviations above baseline, respectively. 2. Mean scores for short-term and long-term recall on the CFT improved also by 1.56 (13.88±8.45 at baseline to 20.13±12.93 at week 12) and 1.38 (14.00±5.60 at baseline to 19.38±11.46 at week 12) standard deviations above baseline, respectively. 3. Perceived memory deficit (RBMT) showed a trend toward improvement over the first 12wk, followed by deterioration after the washout period.

PEDro=Physiotherapy Evidence Database rating scale score (Moseley et al., 2002a)

Discussion

In an RCT, Zhang et al. (2004) demonstrated that donepezil was associated with improvements in tasks of sustained attention and short-term memory, and that these improvements were sustained even after the treatment had finished. Benefits associated with donepezil were also documented in an open-label study by Masanic et al. (2001) who found that the treatment tended to improve both short- and long-term memory of patients living with TBI. Improvements in memory were also reported by Morey et al. (2003) in their retrospective study who demonstrated that donepezil led to significant benefits in visual memory function.

The most recent study, a pre-post by Khateb et al. (2005), found only modest improvement on the various neuropsychological tests used to measure executive function, attention, and learning and memory. Of note results from the learning phase of the Rey Auditory Verbal Memory Test (RAVMT) showed significant improvement ($p<0.050$). The Donepezil intervention also demonstrated improvement in executive function, as the results from the Stroop-colour naming test showed significant improvements ($p<0.030$). On the test for Attentional Performance a significant change was noted on the divided attention (errors) subsection of the test. Overall, donepezil was found to be effective in improving learning, memory, divided attention, and executive function. However, possible benefits of donepezil administration must be balanced against the observed side effects in 27% of the population. Further randomized control trials are required to better explore the efficacy of donepezil post TBI.

Conclusion

There is level 1b evidence that donepezil improves short-term memory compared to placebo post ABI.

There is level 4 evidence that donepezil may be effective in improving short-term, long-term, verbal, and visual memory post ABI.

Donepezil likely improves memory following TBI.

6.2.2.2 Methylphenidate

Methylphenidate is a stimulant which inhibits the reuptake of dopamine and norepinephrine and increases activity in the prefrontal cortex. In the past, methylphenidate has been extensively used as a treatment for attention deficit disorder, as well as narcolepsy (Glenn, 1998). A total of four RCTs examined the efficacy of methylphenidate as a treatment for the recovery of cognitive deficits post ABI.

Table 6.21 The Effect of Methylphenidate on Learning and Memory Post ABI

Author Year Country Research Design PEDro Sample Size	Methods	Outcome
Dymowski et al. (2017) Australia RCT PEDro=9 $N_{Initial}$=11, N_{Final}=10	**Population:** TBI. *Methylphenidate Group (n=6)*: Mean Age=35 yr; Gender: Male=4, Female=2; Mean Time Post Injury=366 d; Mean Worst GCS=4.83. *Placebo Group (n=4)*: Mean Age=32.5 yr; Gender: Male=2, Female=2; Mean Time Post Injury=183.5 d; Mean Worst GCS=4.50. **Treatment:** Participants were randomly assigned to receive either methylphenidate (0.6 mg/kg/d rounded to the nearest 5mg with maximum daily dose of 60 mg) or placebo (lactose). Outcomes relating to processing speed, complex attentional functioning, and everyday attentional behaviour were assessed at baseline, 7-wk (on-drug), 8-wk (off-drug), and 9-mo follow-up. **Outcome Measures:** Symbol Digit Modalities Test (SDMT), Trail Making Test (TMT) A and B; Hayling (A, B, error), Digit Span (DS-Forward, Backward, Sequencing, Total), Ruff 2&7 Selective Attention Test Automatic Speed Raw Score (2&7 ASRS), Ruff 2&7 Selective Attention Test Controlled Speed Raw Score (2&7 CSRS), Simple Selective Attention Task Reaction Time (SSAT RT), Complex Selective Attention Task Reaction Time (CSAT RT), N-back 0-back RT, N-back 1-back RT, N-back 2-back RT, Rating Scale of Attentional Behaviour Significant Other (RSAB SO).	1. After applying Bonferroni corrections, no significant differences between groups from baseline to 7-wk, baseline to 8wk, or baseline to 9-mo were observed for SDMT, TMT A, TMT B, Hayling A, Hayling B, Hayling error, DS Forward, DS Backward, DS Sequencing, DS Total, 2&7 ASRS, 2&7 CSRS, SSAT RT, CSAT RT, N-back 0-back RT, N-back 1-back RT, N-back 2-back RT, or RSAB SO.
Plenger et al. (1996) USA RCT PEDro=5 N=23	**Population:** TBI; Gender: Male=17, Female=6; *Placebo Group (n=13)*: Mean Age=26.6 yr; Mean GCS=8.1; *Methylphenidate Group (n=10)*: Mean Age=31.4 yr; Mean GCS=9.3. **Intervention:** Patients were randomly allocated to receive either methylphenidate or placebo. Methylphenidate was administered at 30 mg/kg, 2 ×/d, for 30 d. **Outcome Measures:** Disability Rating Scale (DRS), Continuous Performance Test (CPT), 2 & 7 Test (2 & 7), Paced Auditory Serial Addition Test (PASAT), Digit Span	1. At 30 d follow-up (n=15), significant differences were obtained on DRS, suggesting better outcome for the methylphenidate group. This difference however was not seen at 90d follow-up (n=11). 2. Significant differences were found on the attention-concentration domain at the 30d follow-up, as indicated by CPT, PASAT, 2 & 7, and Attn/Conc from WMS-R (p<0.030). The treatment group

Author Year Country Research Design PEDro Sample Size	Methods	Outcome
	& Attention/ Concentration from Wechsler Memory Scale-Revised (Attn/Conc from WMS-R).	performed better in these measures compared to the placebo group.
Speech et al. (1993) USA RCT PEDro=7 N=12	**Population:** TBI; Mean Age=27.6 yr; Gender: Male=5, Female=7; Mean Time Post Injury=48.5 mo. **Intervention:** In a crossover design, participants were randomly assigned to receive 0.3 mg/kg methylphenidate, 2 ×/d, for 1-wk, followed by 1-wk of placebo, or receive the treatment in a reverse order. **Outcome Measures:** Gordon Diagnostic System, Digit Symbol and Digit Span subtests of the Wechsler Adult Intelligence Scale-Revised, Stroop Interference Task, Sternberg High Speed Scanning Task, Selective Reminding Test, Serial Digit Test, ++ Katz Adjustment Scale.	1. No significant differences were found between methylphenidate and placebo condition in any of the outcome measures studied.
Gualtieri & Evans (1988) United States RCT Crossover PEDro=7 N=15	**Population:** Mean age=24.1yr; Gender: Male=10, Female=5; Mean time post-injury=46.8mo. **Intervention:** Participants were assigned to receive three conditions in randomized order. 1) Placebo; 2) Methylphenidate (0.15mg/kg) twice daily; 3) Methylphenidate (0.30mg/kg) twice daily. Each condition was 12 days long, with 2 days washout between conditions. **Outcomes:** Adult Activity Scale self-administered (AAS-S), Adult Activity Scale (administrator)(AAS-O), Examiner's Rating Scale (EXRS), Self-Rating Scale (SRS), Verbal Fluency Test (VFT), Non-verbal Fluency test (NVFT).	1. There was a significant improvement in AAS-S and AAS-O scores between the placebo and high-dose conditions ($p<0.05$). 2. There was a significant difference in SRS scores between the placebo group and the high-dose condition ($p<0.05$). 3. On the EXRS there was a significant difference between baseline and low-dose ($p=0.012$), placebo and low-dose ($p=0.025$), baseline and high-dose ($p=0.012$), with higher doses of methylphenidate having improved effects. 4. There was a significant improvement in VFT scores between baseline and the high-dose groups ($p=0.017$). 5. There was a significant difference on NVFT scores between baseline and placebo ($p=0.008$), baseline and low-dose ($p=0.008$), baseline and high-dose ($p=0.008$), and the placebo and high-dose group ($p=0.018$), with methylphenidate improving scores.

PEDro=Physiotherapy Evidence Database rating scale score (Moseley et al., 2002a).

Discussion

Dymowski et al. (2017) investigated the effects of short-term, 7-week, methylphenidate administration (0.6 mg/kg/d) in post TBI patientscompared to a placebo (control). After analysis, it was concluded that there was no significant improvement, or difference between groups for various measures and tests of attention. More than two decades earlier, Speech et al. (1993) conducted a double blind placebo controlled trial evaluating the effects of methylphenidate (0.3 mg/kg, 2 ×/d, for 1 wk,) following closed head injury. Both studies arrived at similar conclusions, as the treatment and placebo group did not vary in any measurements of memory, intelligence, or attention. Conversely, Plenger et al. (1996) found methylphenidate administration (30 mg/kg, 2 x/d, 30 d) significantly improved scores on the Wechsler Memory Scale but for measures of attention and concentration only compared to a placebo. However, the positive results seen by Plenger's group may be due to the use of much higher doses of methylphenidate (30 mg/kg/d vs. 0.6 mg/kg/d for the other studies). Although side effects were unreported, the literature suggests that high doses can lead to acute methylphenidate intoxication; a state comparable to acute amphetamine intoxication, which may cause psychological distress in patients. As a result, the group who most recently published on the topic were likely deterred from increasing the dose past a safely accepted value. Although methylphenidate has been shown to significantly improve measures of attention, no reliable effects on learning and memory have been shown specifically in studies examining ABI populations.

Conclusions

There is level 1b evidence that methylphenidate compared to placebo is not effective for improving memory following brain injury for post TBI patients.

Methylphenidate likely does not improve memory or learning following an ABI.

6.2.2.3 Sertraline

Sertraline, better known under its trade name Zoloft (Pfizer), is a selective serotonin reuptake inhibitor (SSRI) used for the treatment of depression and mood (Khouzam et al., 2003). The majority of sertraline research in the TBI population focuses on the prevention or treatment of major depressive symptoms. However, recent studies have shifted focus and begun to evaluate the benefits of sertraline at improving cognitive disorders (Banos et al., 2010).

Table 6.22 The Effect of Sertraline on Memory and Learning Post ABI

Author Year Country Research Design PEDro Sample Size	Methods	Outcome
Banos et al. (2010) USA RCT PEDro=9 N=99	**Population:** TBI. *Treatment group (n=49)*: Gender: Male=39, Female=10; Mean Age=35.3 yr; Mean Time Post Injury=21.5 d; Mean GCS=5.8. *Placebo group (n=50):* Gender: Male=33, Female=17; Mean Age=34.5 yr; Mean Time Post Injury=19.2 d; Mean GCS=5.8. **Intervention:** Participants were randomized to either the treatment group which took sertraline daily (50 mg) or placebo. Patients were assessed at 3, 6 and 12 months. **Outcome Measure:** Wechsler Memory Index (Wechsler Adult Intelligence Scale III), Symbol-Digit Modalities Test, Logical Memory, Trial Making Test and 64-item Wisconsin Card Sorting Test.	1. More subjects in the treatment group dropped out at each time point. 2. Those in the placebo groups at the 6th and 12th month assessment period were older than the control group and had higher GCS. 3. Overall, there were no significant differences between the two groups on any of the cognitive measures.

PEDro = Physiotherapy Evidence Database rating scale score (Moseley et al., 2002a).

Discussion

The effect of early administration of sertraline on cognitive functioning, intelligence and memory was evaluated by Banos et al. (2010) in an RCT. When comparing the sertraline group, who received 50 mg per day, to a control group (placebo), there were no significant between group differences on any of the neuropsychological tests. The assessments examined attention and concentration, speed of processing, memory, and executive function at 3, 6 and 12 months. Cognitive functioning was not found to improve following the administration of sertraline. Of note, more patients in the sertraline group dropped out of the study compared to the control group when this was quantified at all assessment points— indicating the potential side effects associated with the treatment. Combined with the lack of apparent benefit to using the drug, use of sertraline is not currently recommended.

Conclusions

There is level 1b evidence that sertraline may not improve memory compared to placebo in individuals who have sustained a moderate to severe TBI.

Sertraline has not been shown to improve learning, or memory within the first 12 months post TBI, and may be associated with side effects.

6.2.2.4 Amantadine

Amantadine is a non-competitive N-methyl-D-aspartate receptor antagonist and has been used as an antiviral agent, prophylaxis for influenza A, treatment of neurological diseases such as Parkinson's Disease, and the treatment of neuroleptic side-effects such as dystonia, akinthesia and neuroleptic malignant syndrome (Schneider et al., 1999). Amantadine is also thought to work pre- and post-synaptically by increasing the amount of dopamine in the synapse (Napolitano et al., 2005). Three studies have been identified that investigate the effectiveness of amantadine as a treatment for the remediation of learning and memory deficits and cognitive functioning following TBI.

Table 6.23 The Effect of Amantadine on Learning and Memory Post ABI

Author Year Country Research Design PEDro Sample Size	Methods	Outcome
Hammond et al. (2018) United States RCT PEDro= 9 N=119	**Population:** Mean age=38.6yr; Mean time post-injury=6.2yr; Injury severity: GCS<13. **Intervention:** Individuals were allocated to receive either the placebo or 100mg amantadine twice a day for 60 days. Assessments were completed at baseline, day 28, and day 60. **Outcomes:** Digit-span from Wechsler Memory Scale-III (DS), Trail Making Test (TMT), Controlled Oral Word Association Test (COWAT), Learning/Memory Index (LMI), Attention/Processing Speed Index (APSI).	1. No significant differences were seen on the DS, TMT, COWAT, or the APSI between groups at any time point. 2. The treatment group had significantly lower LMI scores at day 28 compared to the control group (p=0.001), this effect was not present at 60-day follow-up. 3. The treatment group had significantly lower scores on the GCI compared to the control group at day 28 (p=0.002), this effect was not present at day 60 follow-up.
Schneider et al. (1999) USA RCT PEDro=5	**Population:** TBI; Mean Age=31 yr; Gender: Male=7, Female=3; GCS Score Range=3-11. **Intervention:** Patients randomized to either amantadine (50-150 mg 2x/d) or placebo for 2 wk	1. There was a general trend towards improvement in the study sample over the 6 wk. 2. There were no significant between group

Author Year Country Research Design PEDro Sample Size	Methods	Outcome
N=10	in a crossover design with a 2 wk washout period. **Outcome Measure:** Battery of Neuropsychological Tests, Neurobehavioural Rating Scale.	differences in terms of orientation (p=0.062), attention (p=0.325), memory (p=0.341), executive flexibility (p=0.732) or behaviour (p=0.737).
Kraus et al. (2005) USA Pre-Post N=22	**Population:** TBI; Mean Age=36yr; Gender: Male=17, Female=5; Severity of Injury: Mild=6, Moderate=6, Severe=10; Mean Time Post Injury=63.2mo. **Intervention:** Positron emission tomography (PET) scan was done and participants received amantadine (100mg titrated to up to 400mg/d over 3wk). Amantadine was administered 3×/d (200mg at 8AM, 100mg at 12PM, and 100mg at 4PM) for 12wk. **Outcome Measure:** Trail Making Test Part A and B (TMT A, TMT B), Controlled Oral Word Association Test (COWAT), Digit Span, California Verbal Learning Test (CVLT), Rey Osterreith Complex Figure-immediate (Rey Im) and delayed (Rey De) recall.	1. Measures of executive function, as indicated by TMT B and COWAT, were significantly improved in patients following treatment with amantadine (t=-2.47; p<0.02). 2. No significant differences were found for attention (TMT A and Digit Span) or memory (CVLT, Rey Im, and Rey De). 3. Correlational analyses with PET scan results suggest that there may be a strong relationship between executive domain improvement and changes in left pre-frontal metabolism (r=0.92; p=0.01) and left medial temporal metabolism (r=0.91; p=0.01).

PEDro = Physiotherapy Evidence Database rating scale score (Moseley et al., 2002a)

Discussion

In a large sample RCT by Hammond et al. (2018) individuals either received 200 mg of amantadine or placebo for 60 days. Not only was it found that there was no significant effect of amantadine on learning and memory, the control group had significantly higher scores on the Learning and Memory Index (Hammond et al., 2018). In a smaller RCT by Schneider et al. (1999) patients received both placebo and amantadine as well, and no significant effects on learning and memory were found between groups. Similarly, Kraus et al. (2005) demonstrated that the administration of amantadine over a 12-week treatment period does not improve memory deficits or attention; however, significant improvements in executive functioning were observed.

Conclusions

There is level 1b evidence that amantadine does not improve learning and memory deficits in patients post ABI.

Amantadine is not effective for improving learning and memory deficits post ABI.

6.2.2.5 Pramiracetam

Pramiracetam is a nootropic (cognitive) activator that is used to facilitate learning, memory deficiencies, and other cognitive problems. Pramiracetam produces an increased turnover of acetylcholine in hippocampal cholinergic nerve terminals and it is at least 100 times more potent than its original compound piracetam (McLean et al., 1991).

Table 6.24 The Effect of Pramiracetam on Memory Post ABI

Author Year Country Research Design PEDro Sample Size	Methods	Outcomes
McLean Jr. et al. (1991) USA RCT PEDro=5 N=4	**Population:** TBI; Age Range=23-37 yr; Gender: Male=4, Female=0. **Intervention:** Patients were treated in two, 3 wk blocks of oral pramiracetam (400 mg, 2x/d) and placebo over 12wk. **Outcome Measure:** Wechsler Memory Scale (WMS), Selective Reminding Test, Trail Making Test A&B, Finger Tapping Test, Digit Symbol Test, Word Fluency Test.	1. Improvements in immediate and delayed recall in the WMS (logical memory and selecting reminding test) were found for the treatment group. *statistical values not provided in the study

PEDro=Physiotherapy Evidence Database rating scale score (Moseley et al., 2002a).

Discussion

McLean Jr. et al. (1991) conducted a study evaluating Pramiracetam in four males post brain injury. Improvements were found for memory and these improvements remained at one month following discontinuation of the drug. Given the small sample size and the lack of data reported to support the findings, future studies should be conducted.

Conclusions

There is level 2 evidence that pramiracetam may improve males' memory compared to placebo post TBI.

Pramiracetam might improve memory in males post TBI; however, additional studies are required.

6.2.2.6 Physostigmine

Physostigmine is a cholinergic agonist that temporarily inhibits acetylcholinesterase. The inhibition of acetylcholinesterase in turn slows the destruction of acetylcholine, thus increasing the concentration of the neurotransmitter in the synapse. The use of physostigmine in Alzheimer's disease has been examined at length, however it has also been proposed to improve memory in patients with head injury (McLean et al., 1987).

Table 6.25 The Effect of Physostigmine on Memory Post ABI

Author Year Country Research Design PEDro Sample Size	Methods	Outcomes
Cardenas et al. (1994) USA RCT PEDro=6 N=36	**Population:** TBI; Mean Age=29.5 yr; Gender: Male=36, Female=0; Mean GCS=5.31; Mean Time Post Injury=4.33 yr. **Intervention:** Patients randomized to one of 4 treatment protocols: 1) scopolamine, oral physostigmine, washout, placebo (for scopolamine), then placebo (for physostigmine); 2) placebo (for scopolamine), oral physostigmine, washout, scopolamine, then placebo (for physostigmine); 3) placebo (for scopolamine), placebo (for physostigmine), washout, scopolamine, then oral physostigmine; and 4) scopolamine, placebo (for physostigmine), washout, placebo (for scopolamine), then oral physostigmine. Scopolamine was administered at 5 µg/hr via a transdermal patch placed behind the ear. Oral physostigmine was administered initially at 2 mg 3 ×/d, but titrated up to 4 mg 3×/d over 1 wk. Washout period was 1 wk, and each treatment phase lasted 8 d. **Outcome Measure:** Selective Reminding Test (SRT), Wechsler Memory Scale I & II, Digit Symbol, Trail Making Test A & B, Memory Questionnaire, Clinical Balance Tests, Serum Cholinesterase Levels.	1. A total of 16 (44%) participants had improved memory scores while taking oral physostigmine (improvement was defined as >50% increase on Long-term storage or Sum Consistent Long-term Retrieval of the SRT). 2. Participants were divided into either responder (n=16) or non-responder (n=20) groups based on the SRT. 3. Responders showed significantly improved standing time compared to non-responders (p<0.050), suggesting better balance.

PEDro=Physiotherapy Evidence Database rating scale score (Moseley et al., 2002a).

Discussion

In a double-blind, placebo-controlled randomized trial, oral physostigmine was administered to males with TBI as an active treatment (Cardenas et al., 1994). The authors found that physostigmine led to significant improvements in long-term memory scores in 44% (n=16) of study participants. Those who responded favourably to the treatment, as indicated by their performance on the Selective Reminding Test, also demonstrated improved balance compared to non-responders (Cardenas et al., 1994).

Conclusions

There is level 1b evidence that oral physostigmine may improve long-term memory compared to placebo in men with TBI, however more recent studies are required.

Physostigmine may improve long-term memory in men with TBI, however more studies are required.

6.2.2.7 Bromocriptine

Bromocriptine is a dopaminergic agonist which primarily exerts its actions through binding and activating D_2 receptors (Whyte et al., 2008). It has been suggested that dopamine is an important neurotransmitter for prefrontal function, an important area of the brain that contributes to cognitive function, memory, intelligence, language, and visual interpretation (McDowell et al., 1998; Siddiqui et al., 2008). In an animal study looking at the effects of bromocriptine on rats, Kline et al. (2002) noted that the animals showed improvement in working memory and spatial learning; however, this improvement was not seen in motor abilities. Two studies have been identified investigating the use of bromocriptine as an adequate treatment for the recovery of cognitive impairments following TBI.

Table 6.26 The Effect of Bromocriptine on Learning Post ABI

Author Year Country Research Design PEDro Sample Size	Methods	Outcome
McDowell et al. (1998) USA RCT PEDro=4 N=24	**Population:** TBI; Median Age=32.5 yr; Gender: Male=20, Female=4; GCS Range=3-8; Time Post injury Range=27 d-300 mo. **Intervention:** In a crossover design, participants were randomly assigned to receive 2.5 mg bromocriptine (2.5 mg) then placebo or receive treatment in the reverse order. **Outcome Measure:** Dual-task Paradigm (counting and digit span), Stroop Test, Spatial Delayed-response Task, Wisconsin Card Sorting Test (WCST), Reading Span Test, Trail Making Test (TMT), Controlled Oral Word Association Test (COWAT), Control Tasks.	1. Following bromocriptine treatment there were significant improvements on the dual-task counting ($p=0.028$), dual-task digit span ($p=0.016$), TMT ($p=0.013$), Stroop Test ($p=0.050$), COWAT ($p=0.020$), and WCST ($p=0.041$). 2. Bromocriptine had no significant effects on working memory (e.g. spatial delayed-response task and reading span test; $p=0.978$), or on control tasks ($p=0.095$).
Powell et al. (1996) UK Case Series N=11	**Population:** TBI=8, SAH=3; Mean Age=36 yr; Gender: Male=6, Female=5; Time Post Injury Range=2 mo-5 yr. **Intervention:** Patients received bromocriptine (a maximum dose of 5-10 mg/d). Patient assessments included two baseline evaluations (BL1 and BL2), evaluation when stabilized at maximum bromocriptine dose (MAXBROMO), and two post withdrawal evaluations (POST1 and POST2). **Outcome Measure:** Percentage Participation Index (PPI), Spontaneity, Motivation, Card Arranging Reward Responsivity Objective Test (CARROT), Digit Span, Buschke Selective Reminding Test (BSRT), Verbal Fluency, Hospital Anxiety and Depression Scale.	1. Reported PPI ($p<0.0001$), motivation, and spontaneity (both $p<0.005$) increased significantly from BL2 to MAXBROMO. Improvements were seen in CARROT as well ($p<0.0001$). 2. Significant improvements were observed from BL2 to MAXBROMO on the digit span ($p<0.001$), BSRT ($p<0.010$), and verbal fluency ($p<0.001$). Scores on all three tests decreased (non-significant) from MAXBROMO to POST1, scores recovered to near MAXBROMO levels by POST2. 3. Bromocriptine was not associated with improvements in mood state.

PEDro=Physiotherapy Evidence Database rating scale score (Moseley et al., 2002a).

Discussion

The question of whether bromocriptine improves learning and memory in patients with ABI has been explored in one RCT (McDowell et al., 1998; Whyte et al., 2008), and one case series (Powell et al., 1996). In an earlier investigation, low-dose bromocriptine (2.5 mg daily) improved functioning on tests of executive control including a dual task, Trail Making Test, the Stroop test, the Wisconsin Card Sorting Test and the controlled oral word association test (McDowell et al., 1998). However, bromocriptine did not significantly influence working memory tasks, only verbal memory. Although McDowell et al. (1998) demonstrated some benefits following administration of bromocriptine, there was only a single dose administered. Spontaneous recovery may have been a factor leading to the improved abilities in individuals receiving a single dose (2.5 mg daily) of the medication; however, study results did not answer this question. Powell et al. (1996) conducted a multiple baseline design on 11 patients with TBI or subarachnoid hemorrhage who received bromocriptine. Improvements were found on all measures assessed (i.e., verbal memory, attention, motivation spontaneity) except mood. In light of the fact that the last RCT investigating the effects of bromocriptine was conducted 20 years ago, new studies are required to build on the promising results of these very early conclusions.

Conclusions

There is level 2 evidence that bromocriptine may improve verbal memory in individuals with an ABI, however, more studies are required.

More studies are required to determine if the positive effects of bromocriptine on verbal memory seen so far are of potential value.

6.2.2.8 Cerebrolysin

Cerebrolysin has been demonstrated to have neuroprotective and neurotrophic effects and has been linked to increased cognitive performance in an elderly population. As explained by Alvarez et al. (2003), "*Cerebrolysin (*EBEWE Pharma, Unterach, Austria*) is a peptide preparation obtained by standardized enzymatic breakdown of purified brain proteins, and comprises 25% low-molecular weight peptides and free amino acids"* (pg. 272).

Table 6.27 The Effect of Cerebrolysin on Memory Post ABI

Author Year Country Research Design PEDro Sample Size	Methods	Outcomes
Alvarez et al. (2003) Spain Pre-Post N=20	**Population:** TBI; Mean Age=30.1yr; Gender: Male=15, Female=5; Mean GCS=6.1; Time Post Injury Range=23-1107d. **Intervention:** Patients with TBI received a total of 20 intravenous infusions of cerebrolysin solution (30mL/infusion) over 4wk. Assessments were made at baseline, during treatment, and after the 4wk treatment period. **Outcome Measure:** Syndrome Kurztest test (SKT), electroencephalogram (EEG)/brain mapping recordings, and Glasgow Outcome Scale (GOS).	1. Compared to baseline, patients with TBI showed a significant decrease in slow bioelectrical activity frequencies (delta: p<0.01; theta: p<0.05), and a significant increase in fast frequencies (beta: p<0.01) after receiving cerebrolysin, suggesting improvement in brain bioelectrical activity. 2. Significant improvements in SKT performance was noted from pre to post treatment (15.9±2.4 versus 12.0±2.1; p<0.01). 3. GOS scores significantly improved from pre to post treatment (3.7±0.3 versus 3.95±0.3; p<0.05).

Discussion

In an open-label trial of 20 patients with TBI Alvarez et al. (2003) found that cerebrolysin was associated with improved brain bioelectrical activity, as evidenced by a significant increase in fast beta frequencies. A brief neuropsychological battery (Syndrome Kurztest test) consisting of nine subtests was administered to evaluate memory and attentional functions in patients undergoing treatment with cerebrolysin. There was an overall significant improvement in performance post treatment, suggesting patients experienced cognitive benefits from cerebrolysin treatment. Improvements were noted on the Glasgow Outcome Scale as well (Alvarez et al., 2003). Together these findings suggest that cerebroylsin may represent an effective neuroprotective therapy with tangible cognitive benefits for individuals living with an ABI. Controlled trials are necessary to further explore the efficacy of this drug.

Conclusions

There is level 4 evidence that cerebrolysin may improve memory function post ABI.

Cerebrolysin may be beneficial for the improvement of clinical outcome and cognitive functioning following brain injury; however, controlled trials are needed to further evaluate its efficacy.

6.2.2.9 Growth Hormone (GH) Replacement Therapy

Following an ABI, it is not uncommon for individuals to be diagnosed with hypopituitarism. As many as 25 to 40% of individuals with a moderate to severe ABI have demonstrated chronic hypopituitarism (Bondanelli et al., 2007; Kelly et al., 2006; Schneiderman et al., 2008). Despite this, few patients are screened for growth hormone deficiencies; thus, the link between cognitive impairment and growth hormone deficiencies has not yet been definitively established (High et al., 2010). There is very little literature available on the benefits of GH replacement therapy for cognitive deficits after ABI.

Table 6.28 The Effect of rh (GH) on Memory Post ABI

Author Year **Country** **Research Design** **PEDro** ***Sample Size***	**Methods**	**Outcome**
High Jr et al. (2010) USA RCT PEDro=8 N=23	**Population:** TBI. *Placebo* (n=11): Mean Age=39.1yr; Time Post Injury=5.1yr. *Active rhGH* (n=12): Mean Age=36.1yr; Time Post Injury=11yr. **Intervention:** Participants were randomized to either a growth hormone replacement group (rhGH) injection or a placebo injection. Initially the drug was administered at 200*ug*, followed by a 200*ug* increase every month until the dosage reached 600*ug*. Both groups received these injections for one year. **Outcome Measure:** Wechsler Adult Intelligence Scale-III, Delis-Kaplan Executive Function System, California Verbal Learning Test, Wisconsin Card	1. Overall study results did not show great improvements on the majority of assessments between groups. 2. There was a significant improvement on the Finger tapping demonstrated in the treatment group. 3. Processing Speed Index: the treatment group improved significantly over the one-year period ($p<0.05$). The control group showed improvement at the end of the first 6mo ($p<0.01$) but this was not seen at the end of the 1yr. 4. Significant improvement was also noted on the Wisconsin Card Sorting Test

	Sorting Test, Processing Speed Index.	(executive functioning) for the treatment group (p<0.01). 5. On the California Verbal learning Test-II improvement was noted for the treatment group on learning and memory.
Moreau et al. (2013) France PCT N=50	**Population**: TBI. Treatment Group (TG, n=23): Mean Age=37.9yr; Gender: Male=19, Female=4; Mean Time Post Injury=7.8yr; Mean GCS=8.1. Control Group (CG, n=27): Mean Age=37.1yr; Gender: Male=24, Female=3; Mean Time Post Injury=5.5yr; Mean GCS=9.4. **Intervention**: Participants were allocated to receive GH therapy (TG, 0.2-0.6mg/d) or no treatment (CG) for 1yr. Outcomes were assessed before (T1) and after (T2) treatment. **Outcome Measures**: Activities of Daily Living (ADL); Quality of Life Brain Injury (QOLBI); Verbal Memory (VM); Rey Complex Figure (RCF); Reaction Time (RT).	1. Both groups showed significant improvement in instrumental ADL (iADL, p=0.001) at T2, but not personal ADL (pADL). 2. Both groups showed significant improvement in QOLBI total scores (p=0.019) and intellectual (p=0.001), functional (p=0.023), and personal (p=0.044) subscores at T2, but not physical, psychological, and social subscores. 3. Both groups showed significant improvement (p<0.05) in aspects of attention (RT), memory (VM), and visuospatial (RCF) abilities at T2. 4. The TG showed significantly greater improvement in QOLBI functional (p=0.023) and personal (p=0.019) subscores, as well as RCF (p=0.037), but no significant difference was found for other outcome measures. 5. There was a significant correlation (p<0.05) between QOLBI total and pADL (r=0.49). 6. There was a significant negative correlation (p<0.01) between attention (RT) and pADL (r=-0.59) and iADL (r=-0.56).
Reimunde et al. (2011) Spain Cohort N=19	**Population:** TBI; Gender: Male=19, Female=0. With Growth Hormone Deficiency (GHD) Group (n=11): Mean Age=53.36yr; Mean Time Post Injury=44.55mo. Without GHD group (n=8): Mean Age=47.12yr; Mean Time Post Injury=46.6mo. **Intervention:** Those with GHD received recombinant human GH (rhGH), subcutaneously (0.5mg/d for 20d then 1mg/d for 5d). Those without GHD were given a placebo. Cognitive rehabilitation was given to everyone (1hr/d, 5d for 3mo). **Outcome Measure:** Weschler Adult Intelligence Scale (WAIS).	1. Results of the WAIS indicated that the control group improved significantly on the digits and manipulative intelligence quotient (p<0.05). 2. For those in the treatment groups improvement was noted in cognitive parameters: understanding digits, numbers and incomplete figures (p<0.05) and similarities vocabulary, verbal IQ, Manipulative IQ, and total IQ (p<0.01).

PEDro=Physiotherapy Evidence Database rating scale score (Moseley et al., 2002a).

Discussion

A RCT compared the long term (6 months and 1 year) effects of rhGH administration to placebo in a TBI population (High Jr et al. 2010). Significant improvements were noted in processing speed, executive functioning (Wisconsin Card Sorting Test), and learning (California Verbal learning test II) for both the rhGH and placebo groups, with neither group being significantly different from the other. It is important to note while processing speed also improved in both groups at 6 months, the improvement was only sustained in the treatment group at 1 year. Similar results were reported in a more recent PCT by Moreau et al. (2013). Patient quality of life, instrumental activities of daily living, attention, memory and visuospatial ability improved over the treatment period in both the treatment and control group. However, the treatment group improved significantly more in the functional and personal subscales of quality of life assessments, but not memory. Reimunde et al. (2011) performed a cohort study examining the benefits of rhGH administration among those with moderate to severe TBI. Results of the study indicate that those receiving rhGH improved significantly on various cognitive subtests such as: understanding, digits, numbers and incomplete figures ($p<0.05$) as well as “similarities vocabulary”, verbal IQ, Manipulative IQ, and Total IQ ($p<0.01$). The control group also showed significant improvement but only in digits and manipulative intelligence quotient ($p<0.05$). Of note IGF-I levels were similar between both groups at the end of the study.

Conclusions

There is level 1b evidence that recombinant human Growth Hormone (rhGH) is similar to placebo for improving memory and learning in patients post TBI.

There is level 2 evidence that growth hormone (GH) therapy is similar to placebo at improving memory ability in patients post TBI.

The administration of growth hormone complexes likely does not improve learning and memory following an ABI.

6.2.2.10 Rivastigmine

Rivastigmine is an acetylcholinesterase inhibitor which prevents the enzyme acetylcholinesterase from breaking down acetylcholine. This increases the concentration of acetylcholine in synapses. Acetylcholine has been most strongly linked with the hippocampus and memory deficits; however, it is also implicated in attentional processing.

Table 6.29 The Effect of Rivastigmine on Learning and Memory Post ABI

Author Year Country Research Design PEDro Sample Size	Methods	Outcome
Silver et al. (2009) USA RCT PEDro=9 N=127	**Population:** TBI. *Ex-Rivastigmine* (n=65): Mean Age=36.9 yr; Gender: Male=43, Female=22; Time Post Injury=73.5 mo. *Ex-placebo* (n=62): Mean Age=38 yr; Gender: Male=42, Female=20; Time Post Injury=100.1 mo. **Intervention:** Participants were randomized to receive rivastigmine injections (1.5 mg 2x/d to a max of 12 mg/d) or placebo injection. **Outcome Measure:** Trails A and B, Hopkins verbal learning test (HVLT), Cambridge Neuropsychological Test Automated Batter Rapid Visual Information Processing (CANTAB RVIP A).	1. The mean final dose of rivastigmine was 7.9 mg/day. 2. 40% of patients were responders on CANTAB RVIP A’ or HVLT score at week 38. 3. At the end of the study period all (n=98) were seen to improve of the CANTAB RVIP A’ ($p<0.001$), the HVLT ($P<0.001$), and the Trails A and B ($p<0.001$). 4. Further sub-analysis controlling for order effects resulted in no significant differences between groups.

Author Year Country Research Design PEDro Sample Size	Methods	Outcome
Silver et al. (2006) USA RCT PEDro=9 N=123	**Population:** TBI. *Rivastigmine* (n=80): Mean Age=37 yr; Gender: Male=53, Female=27. *Placebo* (n=77): Mean Age=37.1 yr; Gender: Male=53, Female=24. **Intervention:** Participants were randomized to receive either rivastigmine (3-6 mg/d) or placebo. At the end of the first 4 wk, rivastigmine doses were increased to 3.0 mg, 2x/d. If necessary, doses were decreased to 1.5 mg or 4.5 mg 2x/d. **Outcome Measure:** Trails A and B, Hopkins verbal learning test (HVLT), Cambridge Neuropsychological Test Automated Batter Rapid Visual Information Processing (CANTAB RVIP A).	1. Results of the CANTAB RVIP A' and HVLT found no significant differences between the placebo group and the treatment group. 2. Rivastigmine was found to be well tolerated and safe.

PEDro=Physiotherapy Evidence Database rating scale score (Moseley et al., 2002a).

Discussion

In two studies rivastigmine was administered to patients who had sustained a moderate to severe TBI (Silver et al., 2006; Silver et al., 2009). Results from both studies suggest that rivastigmine does not improve memory. In two RCTs Silver et al. (2006;2009) evaluated the effects of rivastigmine on verbal learning. Neither study yielded significant results for any cognitive measures compared to placebo.

Conclusions

There is level 1a evidence that rivastigmine is not effective when compared to placebo for improving memory in ABI populations.

Rivastigmine is not effective in treating memory deficits post ABI.

6.2.2.11 Hyberbaric oxygen therapy

Hyperbaric oxygen therapy involves the inhalation of pure oxygen under pressure allowing the lungs to absorb more oxygen per breath. Currently hyperbaric oxygen therapy is used to treat decompression sickness, serious infections, and delayed wound healing as a result of a comorbid illness such as diabetes (The Mayo Clinic, 2019).

Table 6.30 The Effect of Hyperbaric Oxygen Therapy on Learning and Memory Post ABI

Author Year Country Research Design PEDro Sample Size	Methods	Outcome
Hadanny et al. (2018) Israel	**Population:** Mean age=42.7yr; Gender: Male=58.4%, Female=43.6%; Mean time post-injury=4.6yr; Injury severity: mild=44.8%, moderate=15.6%, severe=39.6%.	1. On measures of general cognitive functioning there was a significant increase in scores after HBOT treatment (p<0.0001).

Case Series N=154	**Intervention:** All individuals received hyperbaric oxygen therapy (HBOT). Sessions consisted of 60-90 mins of 100% oxygen at 1.5/2 ATA exposure 5 days a week. **Outcomes:** NeuroTrax software subsets: general, memory, executive functions, attention, information processing speed, visual spatial processing, motor skills.	2. Memory scores significantly increased following HBOT treatment ($p<0.0001$). 3. Executive function scores significantly increased following HBOT treatment ($p<0.0001$). 4. Attentional scores significantly improved following HBOT treatment ($p<0.0001$). 5. Information processes speed significantly increased following HBOT treatment ($p<0.0001$). 6. Visual spatial processing significantly improved following HBOT treatment ($p=0.005$). 7. Motor skills significantly improved following HBOT treatment ($p<0.0001$).

Discussion

One recent study has evaluated the effects of hyperbaric oxygen therapy on memory deficits following an ABI (Hadanny et al., 2018). The results of this study indicated that hyperbaric oxygen therapy may have positive effects on memory as individuals significantly improved on memory scores following 60-90 minutes of exposure five days a week. It should be noted that this study is retrospective and did not make use of a control group and therefore spontaneous recovery may have influenced recovery.

There is level 4 evidence that hyperbaric oxygen therapy may improve memory following an ABI.

Hyperbaric oxygen therapy may be promising for improving memory following an ABI; however, more controlled studies are required.

6.3 Rehabilitation of Problem Solving, Executive and General Cognitive Functioning

Executive functions refer to higher-level cognitive functions that are primarily mediated by the frontal lobes. These functions include insight, awareness, judgment, planning, organization, problem solving, multi-tasking and working memory (Lezak, 2004). Executive deficits are particularly relevant following traumatic brain injury from both a pathophysiologic as well as a psychosocial perspective. The frontal lobes tend to be one of the brain areas most likely to be injured following trauma (Greenwald et al., 2003). Frequently bilateral frontal lobe injury occurs following TBI which in contrast to typically unilateral insults following vascular injury. Direct contusion to the frontal and temporal lobes can occur but also diffuse axonal injury sustained as a result of TBI affects executive functioning. Patients with a TBI often present with cognitive and behavioral deficits in the presence of little physical impairment.

Cicerone et al. (2000) reviewed 14 studies examining executive functioning and problem-solving (Table 6.13). Only three of the identified studies included a control group and were classified as a randomized controlled trial or non-randomized cohort study.

In later reviews by Cicerone et al. (2005; 2011) 9 and 18 additional studies, respectively, were identified. Some of these studies were not included in our review as they did not meet our inclusion criteria. Based on the results of the studies in their review, Cicerone et al. (2000) recommended, "*training of formal problem-solving strategies and their application to everyday situations and functional activities*".

Executive function deficits are particularly relevant to brain injury survivors who tend to be younger (average age less than 40 years) and who often desire to re-integrate back into pre-injury life roles. Patients with executive function deficits may have the capacity to be independent for basic activities of daily living where actions tend to be more ingrained and one-dimensional. However, instrumental activities of daily living such as banking, scheduling and household activities require intact executive functions due to the increased cognitive complexity and variability of the tasks. Of particular importance are the advanced tasks such as return to driving and competitive employment which are of increased relevance to the younger age demographic associated with TBI (Miller et al., 2003).

6.3.1 Non-Pharmacological Interventions

6.3.1.1 Rehabilitation of Executive Functioning

Within the typical medical and rehabilitation settings, executive function deficits themselves are difficult to identify and evaluate since there is a tendency to focus on other cognitive functions such as memory and attention. It is vital to evaluate interventions for executive functioning as impairment can ultimately hinder successful community re-integration. Further to this, it is also important to address the issue of self-awareness which is particularly important in those who sustain moderate to severe TBI. If individuals are not aware they have a problem, they are less likely to work on compensating for it.

6.3.1.1.1 Individual Interventions

Although executive function deficits post TBI are a common there is little overall research directly addressing the impact of rehabilitation on executive function. Individual interventions aimed at improving executive and general cognitive function are reviewed below.

Table 6.31 The Effect of Individual Therapies on Executive Function Post ABI

Author Year Country Research Design PEDro Sample Size	**Methods**	**Outcome**
Gracey et al. (2017) UK RCT PEDro=6 $N_{Initial}$=74, N_{Final}=59	**Population:** CVA=23, Infection=3, TBI=33, Tumor=10, Missing=1. *Control First (n=34)*: Mean Age=50.18 yr; Gender: Male=23, Female=11; Mean Time Post Injury=8.62 yr. *Assisted Intention Monitoring (AIM, n=36)*: Mean Age=46.36 yr; Gender: males=23, females=13; Mean Time Post Injury=4.89 yr. **Intervention:** Participants were randomized to receive AIM or control first. In the AIM-first group, participants received goal management training followed by text messages for improving achievement of everyday intentions. Control-first group received brain injury information, Tetris game, and non-informational text messages. After 3 wk, participants were crossed over with AIM-first group receiving usual care and control-first	1. Participants achieved a greater proportion of intentions during the AIM intervention relative to control (p=0.040). 2. Participants achieved a greater proportion of goal attainment (without the phone call task) during the AIM intervention relative to control (p=0.033). 3. No significant Group x Time interaction effect was found for the POMS MD or Hotel Test. 4. When only comparing group differences at post-intervention phase 1, intention to treat analysis showed no significant difference between groups for proportion of intentions achieved or

	group receiving AIM. **Outcome Measures:** Mean daily proportion of intentions achieved, Achievement of all goals excluding the phone call task, Profile of Mood States total mood disturbance (POMS MD), Hotel Task, Verbal Fluency.	achievement of goals excluding the phone task.
Lindelov et al. (2017) Denmark RCT PEDro=7 N=68	**Population:** TBI=34, Stroke=20, Other=12, NA=2. *Group A (n=27)*: Mean Age=45.2 yr; Gender: Male=12, Female=15; Mean Time Post Injury=5 yr. *Group B (N=22)*: Mean Age=47.0 yr; Gender: males=8, females=25; Mean Time Post Injury=6.5 yr. *Control Group (n=19)*: Mean Age=54.1 yr; Gender: males=8, females=11; Mean Time Post Injury=7 yr. **Treatment:** Participants were randomly assigned to Group A or Group B; Control group was recruited separately and received no intervention. In Phase 1, Group A received the first version of a targeted hypnosis procedure (improving brain injury or working memory-relating abilities) and Group B received a non-targeted hypnosis procedure (4 weekly 1 h sessions). After a 7 wk break, Phase 2 occurred, with Group A receiving a second version of a targeted hypnosis procedure and Group B receiving the first version of a targeted hypnosis procedure. **Outcome Measure:** Working Memory Index (WMI), B-A Trail Making Index (TMT).	1. In Phase 1, there was significantly more improvement in Group A compared to Group B for WMI (Bayes factor=342) and TMT (Bayes factor=37.5). 2. After the break, the WMI and MT showed no significant differences for either groups compared to before the break. 3. In Phase 2, Group B crossed over to the targeted intervention and showed significant improvements in WMI (Bayes factor=535) and TMT (Bayes factor=72813). Group A showed a small improvement for WMI (Bayes factor=1.5) and TMT (Bayes factor=30). 4. From baseline to last test, there were no significant difference in improvements between Group A and Group B for WMI and TMT.
Powell et al. (2017) USA RCT PEDro=4 N=23	**Population:** TBI=17, Stroke/aneurysm=4, Other=6, More than 1 brain injury=3; Mean Age=44 yr; Gender: Male=11, Female=12; Mean Time Post Injury=4 yr. **Treatment:** Coaches were randomly assigned to ProSolv intervention or usual care. Participants new to the outpatient rehabilitation programme were randomized to coaches and clients already working with coaches were offered the opportunity to participate in the study with that coach. In six 1 h sessions over 8wk, ProSolv group (n=14) received training on using ProSolv app and Usual Care group (n=9) received usual care including training in goal planning/management, time pressure management, and problem-solving skills. ProSolv group had access to the ProSolv app outside of the sessions as a resource for remembering steps to effective problem solving and creating personalized problem-solution lists. **Outcome Measure:** Project-specific knowledge test, Problem Solving Questionnaire (PSQ clear thinking and emotional self-regulation subscales), Problem Solving Rating Scale (PSRS), TBI Self-Efficacy Questionnaire (TBI-SE), Satisfaction with Life Scale (SWLS), System Usability Scale (SUS).	1. No significant differences between groups were found for knowledge test, PSQ clear thinking, PSQ emotional self-regulation, TBI-SE, or SWLS. 2. The average SUS score reported at post-test was 3.5 for the tutorial and 3.6 for the app, suggesting that on average, ProSolv participants were slightly higher than neutral on whether the programme components were usable.

Jacoby et al. (2013) Israel RCT PEDro=7 N=12	**Population:** TBI; *Experimental group (EG; n=6)*: Mean Age=27.83 yr; Gender: Male=4, Female=2; Mean Time Post Injury=126 d; Mean GCS=8. *Control group (CG; n=6)*: Mean Age=30.67 yr; Gender: Male=4, Female=2; Mean Time Post Injury=100 d; Mean GCS=6.25. **Intervention:** Participants were randomly assigned to the EG group or the CG group. All participants in the EG received 10 sessions of virtual reality (VR) training (45 min/session, 3-4 x/wk). The CG received general cognitive re-training treatment identical in length and duration to the EG. **Outcome Measure:** Multiple Errands Test – Simplified Version (MET-SV), Executive Function Performance Test (EFPT).	1. Participants in the EG group improved more in their final scores on the MET-SV relative to their initial scores compared to the CG group (p=0.046). 2. Participants in the EG improved more in their final scores on the EFPT relative to their initial scores compared to the CG (p=0.046). 3. Between group differences showed no significant difference at baseline.
Man et al. (2013) Hong Kong RCT PEDro=4 N=40	**Population:** TBI. Age Range=18-55yr; Gender: Unspecified; Time Post Injury: Unspecified; Mean GCS=10. **Intervention:** Participants received twelve 20-25 minute sessions of a vocational problem-solving skill training program. Participants were randomized to either artificial intelligence virtual reality (treatment group, TG) or conventional psychoeducation (control group, CG). Outcomes were assessed before and after treatment, and at follow-up of 1, 3, and 6 months. **Outcome Measures:** Wisconsin Card Sorting Test (WCST); Tower of London Test (TLT); Vocational Cognitive Rating Scale (VCRS); Self efficacy (SE); Vocational outcomes.	1. Both groups showed significant improvements on WCST, TLT, VCRS, SE, and vocational outcomes after treatment compared to baseline ($p<0.050$). 2. On WCST, the TG performed better than the CG after treatment ($p\leq0.020$). No other significant between-group differences were found.
Couillet et al. (2010) France RCT PEDro=5 N=12	**Population:** severe TBI; Gender: Male=9, Female=3. *Group 1 (n=5)*: Mean Age=23.8 yr; Mean GCS=4.8; Mean Time Post Injury=6.3 mo. *Group 2 (n=7)*: Mean Age=26.7 yr; Mean GCS=4.8; Mean Time Post Injury=16.1 mo. **Intervention:** Randomized AB versus BA design, where "A" represents the control phase and "B" represents the treatment (dual-task training) phase. In the dual-task phase, patients were trained to conduct two concurrent tasks simultaneously. Group 1 started with the control phase (AB) and Group 2 (BA) with the treatment phase. Each phase lasted 6 wk (4, 1 hr sessions/wk). **Outcome Measure:** Test Battery for Attentional Performance (TAP: divided attention and flexibility subtests), Go-no go and Digit Span, Trail Making Test, Stroop Test, Brown-Peterson Paradigm, Rating Scale of Attentional Behaviour.	1. Following training, there was a significant improvement in the 2 tasks that targeted divided attention (TAP-divided attention, Go-no go and Digit Span: $p<0.0001$ for both). 2. The two groups differed significantly at 6 wk with those in the BA design doing better on TAP reaction times ($p<0.010$), the digit span dual-task ($p<0.001$), and the Rating Scale of Attentional Behaviour ($p<0.010$). 3. There was a significant difference between groups at 6 wks on the Stroop test ($p<0.001$) and the flexibility subtest of the TAP ($p<0.001$), but not the Trail Making Test or the Brown-Peterson task. 4. Experimental training had no significant effects on non-target measures.
Spikman et al. (2010) Netherlands RCT PEDro=7 N=75	**Population:** Mean Age: 42.5 yr; Gender: male=50, female=25; Condition: TBI=33, Stroke=32, Other=10. **Intervention:** Individuals were randomly assigned to either the experimental group which comprised of multifaceted strategy	1. The experimental group improved significantly more over time than the controls on the RRL and attained significantly higher scores on the TGA and EST ($p<0.010$).

	training (n=38) or the control group (n=37). The primary goal of the treatment group was to improve 8 aspects of executive functioning. **Outcome Measure:** Role resumption list (RRL); treatment goal attainment (TGA) and Executive Secretarial Task (EST).	
Levack et al. (2009) (Levack et al., 2009) New Zealand RCT PEDro=5 N=34	**Population:** *GMT (N=12):* Median age=29; Gender: Male=10, Female=2; Median time post-injury=5yr. *IOGT (N=10):* Median age=28yr; Gender: Male=9, Female; Median time post-injury=5yr. *Usual Care (N=12)*: Median age=40; Gender: Male=8, Female=4; Median time post-injury=7. **Intervention:** Individuals were assigned to either no treatment, goal management training, or identity oriented goal training. **Outcomes:** Goal Attainment Scale, behavioral observations.	1. All groups improved GAS scores over the course of treatment and at follow-up. The greatest improvement in scores was seen in the usual care group. Observationally both clinicians and participants reported feeling positively about the efficacy of GMT, and its ability to improve goal execution, multitasking, and time management.
Constantinidou et al. (2008) United States RCT PEDro=8 N=14	**Population:** *Experimental Group (N=21)*: Mean age=32.1yr; Mean time post-injury=9.74 mo. *Control Group (N=14)*: Mean age=27.57yr; Mean time post-injury=10.55 yr. **Intervention:** Individuals received either the Categorization Program intervention for 13 weeks averaging 4.5 hours of therapy per week, or 'regular therapy' (control group). **Outcomes:** CP Test 1 (object recognition/memory), CP Test 2 (executive functioning), CP Probe Tasks (executive functioning), Community Reintegration Questionnaire (CIQ), Mayo-Portland Adaptability Inventory (MPAI-3), California Verbal Learning Test (CVLT), Rey Complex Figure Test (RCF), Wechsler Memory Scale (WMS-III), Woodcock Johnson (WJ-III), Scales of Cognitive Ability for Traumatic Brain Injury (SCATBI).	1. The experimental group significantly improved on CP Test 1 (object recognition) compared to the control group (p=0.039). 2. Individuals in the experimental group performed significantly better on the CP Test 2 (executive functioning) compared to the control group post-intervention (p=0.010). 3. Individuals in the experimental group performed significantly better on the probe tasks, compared to controls, post-treatment (p=0.008). 4. Individuals in both groups significantly improved performance on the CIQ and MPAI-3 (p<0.05). 5. The experimental group had greater improvement on the CVLT-R. 6. There were no differences in scores between groups on the RCF, WMS-III, WJ-III, SCATBI.
Levine et al. (2000) Canada UK RCT PEDro=4 N=30	**Population:** TBI: *Goal Management Training (GMT) Group* (n=15): Mean Age=29.0 yr; Gender: Male=5, Female=10; Mean GCS=10.7; Mean Time Post Injury=3.7 yr. *Motor Skill Training (MST) Group* (n=15): Mean Age=30.8 yr; Gender: Male=9, Female=6; Mean GCS=10.8; Mean Time Post Injury=3.8 yr. **Intervention:** Patients were randomized into the GMT or MST group. The GMT was comprised of five steps: 1) orienting and alerting to task, 2) goal selection, 3) partitioning goals into sub-goals, 4) encoding and retention of sub-goals, and 5) monitoring. The MST was training that was unrelated to goal management: reading and tracing mirror-reversed text and designs. Participants were tested on everyday paper and pencil tasks that	Everyday paper and pencil Task 1. The GMT group compared to the MST group had significantly greater accuracy on the everyday paper and pencil tasks post-training (p<0.050). 2. The MST group also had significantly more errors during the everyday paper and pencil tasks (p<0.010). 3. The GMT group significantly reduced their errors from pre-post training during the everyday paper and pencil tasks (p<0.010). 4. The GMT also devoted significantly more time to proofreading and the room-layout tasks than the MST group from pre to post-training (p<0.050). Neuropsychological Tasks

	focused on holding goals in mind, sub-goal analysis and monitoring. **Outcome Measure:** Goal Neglect (Everyday paper and pencil tasks), Stroop Interference Procedure, Trail Making A and B, Wechsler Adult Intelligence Scale Revised (WAIS-R).	1. The GMT group was generally slower on timed neuropsychological tests: Stroop Interference Procedure, Trail Making Part A and B ($p<0.050$ and $p<0.060$, respectively). 2. No significant differences between groups for the WAIS-R ($p>0.050$).
Sohlberg et al. (2000) USA PEDro=8 N=14	**Population:** TBI=11, ABI=1, Other=2. *Attention Process Training (APT) Group (n=7)*: Mean Age=33.1 yr; Mean Time Post Injury=7.5 yr; *Control Group (n=7)*: Mean Age=38.1 yr; Mean Time Post Injury=1.6 yr. **Intervention:** Patients were randomized to receive either the APT training (treatment) or the brain injury education and supportive listening (control), in a cross over design. APT was 24 hr over 10 wk and the control group received 10 hr over 10 wk. All subjects worked directly with a therapist and assessed pre and post intervention. **Outcome Measure:** Trail Making Test, Paced Auditory Serial Addition Task (PASAT), Gordon Diagnostic Vigilance and Distraction, Controlled Oral Word Association Task (COWAT), Stroop Task, Attention Questionnaire.	1. Those in the APT group reported significantly more changes than the control group (0.91 and 0.58 respectively, $p<0.050$). 2. The effect of type of change was significant ($p<0.0001$); a greater number of memory/ attention changes were reported for the APT group, whereas more psychological changes were reported for the control. 3. Changes in PASAT scores corresponded with perceived cognitive improvement in the interview; changes in PASAT scores were greater for those who reported >2 cognitive changes ($p<0.050$). 4. Results of the PASAT, Stroop Task, Trail Making Test B, and COWAT also found that those with higher levels of vigilance had improved scores ($p<0.01$). 5. For the aforementioned tasks, there were also specific improvements in performance associated with APT that were greater than those associated with brain injury education ($p<0.050$).
Webb & Glueckauf (Webb & Glueckauf, 1994) United States RCT PEDro=6 N=16	**Population:** Mean age=27.4yr; Mean time post-injury=8.7yr; Mean coma duration=88.9dy. **Intervention:** Participants were randomly assigned to a high involvement goals setting program or a low involvement program for 8 weeks meeting 1 hour per week. Individuals were assessed pre-intervention, post-intervention, and at 2-month follow-up. **Outcomes:** Goal Attainment Scale (GAS).	1. There were no significant between group differences at baseline. 2. Both groups significantly improved on the GAS over time regardless of condition ($p<0.001$) post-treatment. 3. The high involvement group showed significant additional gains on the GAS compared to the low involvement group at 2-month follow-up ($p<0.05$).
Holleman et al. (2018) Netherlands PCT N=75	**Population:** *Experimental Group (N=42):* Mean age=43.3yr; Gender: Male=27, Female=15; Mean time post-injury=7.9yr. *Control Group (N=33)*: Mean age=40.7yr; Gender: Male=20, Female=13; Mean time post-injury=6.9yr. **Intervention:** Participants were either assigned to the Intensive NeuroRehabilitation programme or the control group. The programme took place over the course of 16 weeks and consisted of 2 groups of 7 weeks of training with a 2-week break in between. Individuals had 5 hours of training 4 days a week in a group setting. **Outcomes:** Symptom checklist (SCL), Beck Depression Inventory-II (BDI-II), Hospital Anxiety and Depression Scale (HADS),	1. There were no significant between group differences pre-intervention on any measures. 2. Following the intervention, the experimental group had significantly lower SCL scores indicating a reduction in overall symptoms ($p=0.005$). 3. On measures of neuropsychological functioning, the experimental group reported significantly lower scores on the BDI-II ($p=0.001$), HADS ($p<0.01$), and ZBV-trait ($p=0.002$) showing improvement on these neuropsychological measures.

	Zelfbeeldenvragenlijst-trait (ZBV), Quality of Life in Brain Injury (QOLIBRI), Trail making test Part A, Stroop test, Wechsler Adult Intelligence Scale-III (WAIS-III), Rey Auditory Verbal Learning Test, Rivermead Behavioural Memory Test, Groninger Intelligentie Test 2, Trail making test Part B.	4. The experimental group reported significantly higher scores for quality of life on the QOLIBRI ($p<0.05$). 5. On measures of cognitive functioning no significant differences were seen for any outcome measures.
Kim et al. (2018) United States Pre-post N=13	**Population:** Median age=40yrs; Gender: Male=7, Female=6; Median time post-injury=23yr. **Intervention:** Heart rate variability biofeedback training was conducted for 10 1-hour sessions. After the fourth session individuals were given a portable biofeedback device to take home and self-monitor. **Outcomes:** Category Test (CT), Heart rate variability index (HRV), Positive Affect and Negative Affect Schedule (PANAS).	1. HRV biofeedback significantly improved CT scores ($p<0.05$), this effect was magnified by those experiencing positive affects during treatment as measured by the PANAS. 2. No other significant results were found.
Dahdah et al. (2017) USA Pre-Post $N_{Initial}$=21 N_{Final}=15	**Population:** CVA=6, TBI=5, Tumor=2, Anoxia brain injury=2; Mean Age=40.3 yr; Gender: Male=12, Female=3. **Treatment:** Participants received the virtual reality (VR) intervention sessions (apartment and classroom) twice per week for a 4 wk period. Sessions 1 and 8 included all types of distractors, sessions 2 and 3 included no distracting stimuli, sessions 4 and 5 included only auditory distracting stimuli, and sessions 6 and 7 included only visual distracting stimuli. **Outcome Measure:** Woodcock-Johnson, 3rd edition (WJ-III pair cancellation subtest), Delis-Kaplan Executive Function System (D-KEFS Color-Word Interference subtest), Automated Neuropsychological Assessment Metrics (ANAM Go/No-Go and unimodal Stroop subtests), VR Stroop task (apartment and classroom).	1. No statistically significant performance differences were found from baseline to conclusion of the study for the VR apartment Stroop or D-KEFS Stroop test. 2. For the VR classroom, participants' shortest response time on the word-reading condition was significantly reduced by session 8 ($p=0.0383$). All other VR classroom Stroop variables did not show significant differences. 3. No significant differences from session 1 to session 8 were found for all pair cancellation subtest scores. 4. From session 1 to 8, the ANAM Stroop word-reading percentage of items with a correct response ($p=0.0293$), ANAM Stroop word-reading number of correct responses per minute ($p=0.0321$), and ANAM Go/No-Go number of impulsive/bad responses ($p=0.0408$) significantly increased. All other ANAM variables did not show significant differences.
O'Neil-Pirozzi and Hsu (2016) PCT $N_{Initial}$=14 N_{Final}=12	**Population:** TBI=4, CVA=2, Brain tumour=1; Severity: moderate/severe. *Experimental Group (n=7)*: Mean Age=51.3 yr; Gender: Male=5, Female=2; Mean Time Post Injury=20.9 yr; Etiology: TBI=5, CVA=2. *Control Group (n=7):* Mean Age=46.9 yr; Gender: Male=7; Mean Time Post Injury=25.0 yr. **Treatment:** Experimental group participants received BrainHQ, a commercially available online computerized cognitive exercise program (Attention, Brain Speed, Memory, People Skills, Intelligence, and Navigation) for 5 mo, 5 d/wk. Control group participants did not have a private computer and received no intervention. **Outcome Measure:** Number/Percentage of Sessions Completed, Number/Percentage of	1. Of the five experimental group participants that completed the study, they completed an average 87% of sessions, initiated an average 25% of sessions, and independently completed an average 7% of sessions. Two participants needed minimum external cues, two participants needed moderate external cures, and one participant needed maximum external cues. 2. Comparing 3 mo prior to intervention with 1 wk prior to intervention, there were no significant differences within either group for WCST, HVLT-R, COWAT, TMT A or B, or SWLS. 3. There were no significant differences between groups at 1 wk prior to

	Sessions Initiated by Participants, Number/Percentage of Sessions Completed Independently by Participants, Mean Amount of External Cures Provided for Session Completion, Wisconsin Card Sorting Test (WCST), Hopkins Verbal Learning Test-Revised (HVLT-R immediate, delayed), Controlled Oral Word Association Test-FAS (COWAT), Trail Making Test (TMT A and B accuracy and speed), Satisfaction with Life Scale (SWLS), Semi-structured interview questions.	intervention (baseline) for WCST, HVLT-R, COWAT, TMT A or B, or SWLS. 4. Compared to baseline, experimental group showed significant improvement post-intervention for HVLT-immediate (p=0.0255) and SWLS (p=0.0075). There were no significant improvements for WCST, HVLT-delayed, or TMT A or B. 5. Compared to baseline, control group did not show significant differences post-intervention for WCST, HVLT, TMT A or B, or SWL. 6. Compared to control group, experimental group showed significantly higher post-intervention improvements on HVLT-immediate (p=0.0068) and COWAT (p=0.0310). No significant differences between groups were found for changes in WCST, HVLT-delayed, TMT A or B, or SWL. 7. Of the experimental group participants who completed the study, 60% reported improved everyday thinking abilities, 60% reported improved memory, and 20% reported improved attention, organization, and/or problem solving skills, but 60% reported they would not continue with exercise program post-study completion.
Li et al. (2015) USA Pre-Post $N_{Initial}$=13 N_{Final}=12	**Population:** Stroke=5, TBI=5, Brain tumor=2; Mean Age=61 yr; Gender: Male=10, Female=2. **Treatment:** Participants received the computer-based cognitive retraining program, Parrot Software. The following eight modules were each completed in separate 1 h sessions: Visual Instructions, Attention Perception and Discrimination, Concentration, and Visual Attention Training, Remembering Written Directions, Remembering Visual Patterns, Remembering Written Letters, and Remembering Written Numbers. **Outcome Measure:** Montreal Cognitive Assessment (MoCA overall, attention, memory), Medication-box sorting task.	1. Compared to baseline, there was a significant mean increase in overall MoCA of 3.25 (p=0.030) post-intervention. However, the attention and memory subscales did not show significant differences. 2. There were no significant differences before and after intervention for the medication-box sorting task. 3. Participants with previous computer-based cognitive retraining experience had significantly more MoCA improvement than those without (p<0.010). 4. Age, education level, or type of ABI diagnosis did not have any significant effects on MoCA or medication-box scores.
Fong & Howie (2009) China PCT N=33	**Population:** Mean age=33.4yr; Gender: Male=27, Female=6; Mean time post-injury=12.3 mo. **Intervention:** The experimental group received an enhanced cognitive training program in addition to the standard cognitive rehabilitation training program received by the control group. **Outcomes:** Key Search test, Social Problem-Solving Video Measure (SPSVM), Means-Ends Problem-Solving Measure (MEPSM), Raven's	1. No significant differences were found on the Key Search test, the SPSVM, RPM, or the MEPSM between groups following intervention. 2. There were significant between group differences on two of the categories for the MI; correctness of representation scores (p=0.041), and total average correct scores (p=0.009). No other significant differences were found.

	Progressive Matrices (RPM), Metacomponential Interview (MI).	
Laatsch et al. (1999) USA Case Series N=5	**Population:** TBI; Age Range=18-65 yr; Time Post-Injury=2-48 months; **Intervention:** Cognitive rehabilitation therapy (CRT) programme in a longitudinal protocol involving a resting SPECT and neuropsychological evaluation are pre-treatment, post-treatment and post non-treatment intervals. **Outcome Measure:** Neuropsychological measures.	1. NP measures: WAIS-R, WMS-R, CVLT, RCFT, SCWT, WCST or ACT, SPECT image. 2. SPECT data revealed significant increases in cerebral blood flow during the treatment period (p<0.050). 3. CRT was found to be effective in improving both NP and everyday functioning. All patients were able to be more productive in their lives following treatment.
Chen et al. (1997) USA Case-Control N=40	**Population:** Age=18+ yr; Gender: male=27, female=13; Condition: TBI. **Intervention:** Divided retrospectively into computer-assisted rehabilitation (CACR) and tradition therapy groups **Outcome Measure:** Neurophysiological Test Scores (WAIS-R; WMS).	1. Both groups made significant post-treatment gains on the neurophysiological test scores (p<0.050), with the CACR group making significant gains on 15 measures (p<0.050) and the comparison group making significant gains on seven measures (p<0.005). 2. However, no significant difference was found between groups on their post-treatment gains.
Freeman et al. (1992) United States PCT N=12	**Population:** *Experimental Group (N=6):* Mean age=38.5yr; Mean time post-injury=33.33mo. *Control Group (N=6)*: Mean age=47.83yr; Mean time post-injury=11.83mo. **Intervention:** The intervention consisted of being enrolled in a 6-month cognitive rehabilitation programme which met 3x weekly, for 2 hours. The control group received no such treatment. **Outcomes:** Wechsler Adult Intelligence Scale for Children (WAIS-R)	1. Post-intervention the experimental group was seen to have significantly improved scores on the WAIS-R compared to the control group (p=0.02).

Discussion

The effects of hypnosis, as delivered in a targeted or non targeted manner, on memory, attention, and cognitive function in a mixed TBI and stroke population has been investigated (Lindelov et al. 2017). The researchers showed that working memory, attention, and cognitive function could be transiently increased during targeted hypnosis; however, the benefits of the treatment were not sustained when the treatment was discontinued. With respect to attention process training, it was shown that this intervention may have indirectly improved executive function as individuals with higher vigilance achieved higher executive function scores, but it was not explicitly demonstrated that training resulted in increased vigilance (Sohlberg et al., 2000).

Dual-task training which is also used as a form of attention training was also evaluated in another RCT and although individuals were improved on measures of attention to a significantly greater extent than controls, no such relationship was found for measures of executive function (Couillet et al., 2010).

With the development of technology, the use of virtual-reality training and computer programs have gained traction as an intriguing tool used for improving executive function in patients post TBI. In terms of cognitive functioning, two RCTs found varying results for executive functioning outcomes after training in a virtual environment (Jacoby et al., 2013; Man et al., 2013). One RCT focusing on vocational problem-solving skills (Man et al., 2013) identified significant improvements in both VR intervention and conventional psychoeducation control groups; however, there were no significant between-group differences for cognitive or vocational outcomes except on WCST % errors and % conceptual level response (Man et al., 2013). Conversely, Jacoby et al (2013) found that patients receiving virtual reality training improved more on multi-tasking measures and executive function when compared to the control group who received general cognitive re-training treatment. In a pre-post study, Dadah et al. (2017) investigated virtual reality interventions in a mixed ABI population. The researchers found that repetition of the Stroop test in different virtual reality environments showed limited improvement in performance on those specific tests (Dahdah et al., 2017). As a result of the mixed results reported on the efficacy of virtual reality training post ABI, it is difficult to make a conclusive decision on what aspects of executive functioning virtual reality benefits, and to what degree.

As previously mentioned, computer software programs have also been investigated for their efficacy in improving executive dysfunctions post TBI. Recently, BrainHQ, a commercially available online computerized cognitive exercise program, showed mixed results for improving executive function post ABI (O'Neil-Pirozzi & Hsu, 2016). Although individuals self-reported improvements in daily functioning, no significant results were seen on objective measures (O'Neil 2016). Parrot Software is another computer-based cognitive retraining program, and was investigated by a pre-post study assessing the efficacy of using eight modules focussed on attention and memory (Li et al., 2015; Li et al., 2013). While significant post-treatment improvements in attention and memory on the Cognistat assessment were found in a pilot study (Li et al., 2013), a subsequent study did not find significant improvements on the Montreal Cognitive Assessment (MoCA) or a medication-box sorting task despite significantly improved overall MoCA scores (Li et al., 2015). This lack of improvement compared to a control group was also reported by Powell et al. (2017) when the ProSolv smartphone application was used to improved pressure management and problem-solving skills. Finally, Chen et al. (1997) studied the effect of computer assisted cognitive rehabilitation versus traditional therapy methods. While measures of attention significantly improved in both groups after treatment, no significant differences were observed between groups on any measures related to executive function (Chen et al., 1997). Cumulatively, by observing studies from across a period of nearly 20 years, the literature reveals little support for the use of computer software programs for the improvement of executive function post TBI.

In an RCT, Spikman et al. (2010) randomly divided a group of individuals who had sustained a TBI to either a multifaceted strategy training group or a control group. Those in the treatment group were taught a comprehensive cognitive strategy which allowed them to tackle the issues and problems of daily living, compared to the control group which received a computerized training package that was aimed at improving general cognitive functioning. Overall, results indicate both groups improved on many aspects of executive functioning; however, those in the treatment group showed greater improvement in their ability to set and accomplish realistic goals and to plan and initiate real life tasks (Spikman et al., 2010). The findings of the previous experiment agree with the findings of the study by Laatsch et al. (1999) and Freeman et al. (1992), where cognitive rehabilitation therapy was found to increase productivity and everyday functioning. This older study (Laatsch et al., 1999) also had the benefit of reporting SPECT imaging results, which revealed increases in cerebral blood flow during the intervention. It should be noted that one study has found mixed results on measures of executive functioning after administering a cognitive training program, with individuals improving on some measures of executive functioning, such as metacognition, but not others (Fong & Howie, 2009). It should be noted that none of the above studies were completed by the same groups or had overlapping methodology and although the results suggest cognitive training programs are effective for improving executive functioning following an ABI, programs themselves should be considered unique.

A specific cognitive program (Categorization Program) was evaluated in an RCT by Constantinidou et al. (2008). The authors found that after 13 weeks of therapy (mean 4.5 hr/day), individuals significantly improved on measures of executive functioning such as object recognition. Although the Categorization Program treatment group and standard therapy therapy group showed improvement on the community reintegration questionnaire and adaptability measures, there were greater executive function gains in the treatment group (Constantinidou et al., 2008). The Intensive NeuroRehabilitation Programme investigated by Holleman et al. (2018) resulted in significantly reduced depression and anxiety compared to the control group but did not improve measures of executive functioning.

Another unique study used heart rate variability biofeedback in an attempt to increase awareness and cognitive control (Kim et al., 2018). In this study it was noted that individuals who underwent heart rate biofeedback significantly improved scores of executive functioning on the Category Test. However, this study consisted of a pre-post design and lacked a control group for comparison, and as such results should be interpreted with caution.

Levine et al. (2000) completed an RCT comparing a group of patients using goal management training strategies to a control group who were received only motor skills training. The treatment group improved on paper and pencil everyday tasks as well as meal preparation-which the authors used as an example of a task heavily reliant on self-regulation in comparison to the motor treatment group. It is important to note, however, that the motor group performed superiorly on timed neuropsychological tests, and no differences were found between treatments in terms of intelligence. A second study also evaluating goal management training in 2009 and did not find any significant results suggesting that goal management training improves executive functioning following an ABI (Levack et al., 2009). A single older study reported positive affects of a goal setting program in its ability to help an individual achieve goals (Webb & Glueckauf, 1994). The execution of goals themselves requires executive functioning; however, no objective measures of executive function were directly evaluated in this study.

Conclusions

There is level 1b evidence that targeted hypnosis may transiently improve cognitive function in post TBI patientsor stroke.

There is level 1b evidence that an attention remediation intervention may not be superior to TBI education alone and improving executive function in patients post TBI.

There is level 2 evidence that dual-task training may improve not general cognitive functioning compared to a non-specific cognitive program in patients post TBI.

There is level 1b evidence that a comprehensive cognitive treatment strategy programs (which include problem solving), compared to controls, are effective for improving metacognition and goal achievement post TBI.

There is level 4 evidence that cognitive rehabilitation may increase productivity in everyday functioning, and cerebral blood flow during treatment in patients post TBI.

There is level 1b evidence that virtual-reality training is not superior to conventional cognitive training at improving cognitive and executive function outcomes post TBI.

There is level 1b evidence that the specific cognitive training program ProSolv, compared to standard therapy, does not improve measures of executive functioning following an ABI.

There is level 2 evidence that the Intensive NeuroRehabilitation programme, compared to no treatment, does not improve executive functioning following an ABI.

There is level 2 evidence that computer or smartphone software programs, such as BrainHQ, Parrot Software, ProSolv app, may not be superior to no intervention at improving problem-solving skills and general functioning in patients post TBI.

There is level 4 evidence that heart rate biofeedback may improve executive functioning following an ABI, although higher level studies are required to fully determine this.

There is level 2 evidence that goal management training may be superior (compared to motor skills training or no treatment controls) for improving goal attainment or measures of intelligence following an ABI.

Targeted hypnosis may improve memory, attention, and cognitive function in post TBI patientsor stroke; however, only as long as the intervention is being administered.

Attention training programs likely do not improve executive functioning.

General cognitive training programs which include problem-solving appear to be effective for improving executive functioning following an ABI.

Virtual reality does not likely improve executive functioning following an ABI.

Computer or smartphone software programs (BrainHQ, Parrot Software, ProSolv app) may not be superior to common interventions at improving memory, attention, and problem-solving skills in patients post TBI.

Goal management training may be superior to motor skills training at improving everyday skills (meal preparation), but not intelligence or neuropsychological outcomes in patients post TBI.

Heart rate variability biofeedback may improve executive functions; however, more controlled studies are required to make further conclusions.

6.3.1.1.2 Group-based Interventions

Although executive function deficits are a common there is little overall research directly addressing the impact of rehabilitation on executive function. However, community integration and other similar group-based interventions are highly related to executive function and it is possible that programs and interventions presented in a group-based setting may in fact be focusing efforts on instrumental activities of daily living which may reflect (or are dependent on) executive functions. The efficacy of group-based interventions on cognitive and executive function are discussed below.

Table 6.32 The Effects of Group Therapy on Executive Function Post ABI

Author Year Country Research Design PEDro Sample Size	Methods	Outcome
Tornas et al. (2016) Norway RCT PEDro=9 $N_{Initial}$=70, N_{Final}=67	**Population:** TBI=45, Stroke=15, Tumour=6, Anoxia=2, Other=2. Mean Age=42.89 yr; Gender: Male=38, Female=32; Mean Time Post Injury=97.47 mo. **Intervention:** Participants were randomized to receive Goal Management Training (TG) or Brain Health Workshop (CG) group sessions. GMT group (n=33) discussed distinctions between absentmindedness/presentmindedness, slip-ups in daily life, habitual responding, stopping and thinking, working memory, importance of goals, defining/splitting goals into subtasks, and checking. BHW control group (n=37) discussed brain function/dysfunction, brain plasticity, memory, executive function, and attention. Treatment was received one day every second week, for a total of eight two-hour sessions distributed over four days. Outcomes were assessed at baseline (T1), after treatment (T2), and at six-month follow-up (T3). **Outcome Measures:** Behaviour Rating Inventory of Executive Function–Adult (BRIEF-A); Dysexecutive Questionnaire (DEX); Cognitive Failures Questionnaire (CFQ); Continuous Performance Test II (CPT-II); UCSD Performance-Based Skills Assessment (UPSA); Delis-Kaplan Executive Function System Battery–Colour-Word Interference Test (CWI), Verbal Fluency Test (VFT), and Tower Test (TT); Trail Making Test (TMT); Hotel Task (HT).	1. In the TG, significant improvements were found on BRIEF-A, DEX, and CFQ at T3 (p<0.010). 2. In the CG, significant improvements were found on only BRIEF-A at T2 (p<0.050). 3. The TG showed significant improvements on BRIEF-A and DEX (p<0.010), but not CFQ, compared to the CG over time 4. In the TG, significant improvements were found on CPT-II, CWI, TT, and HT at T2 and T3 (p<0.050), VFT at T3 (p<0.050), and UPSA at T2 (p<0.001). 5. In the CG, significant improvements were found on CPT-II, TT, and HT at T2 and T3 (p<0.050), and VFT and UPSA at T2 (p<0.050). 6. The TG showed a significant improvement on CWI, VFT, and TT (p<0.050), but not CPT-II, UPSA, and HT, compared to the CG over time. 7. No significant differences were found on TMT within or between groups over time.
Cantor et al. (2014) USA RCT PEDro=6 N=98	**Population:** TBI; Mean Age=45.3 yr; Gender: Male=37, Female=61; Mean Time Post Injury=12.6 yr; Severity: Mild=49, Moderate=19, Severe=30. **Intervention:** Participants were randomly assigned to either immediate start (IS; n=49) or waitlist control (WL; n=49) groups. Participants received group sessions of emotional regulation (2 sessions, 45 min) and an individual problem-solving session of attention training (1 session, 60 min) per day (3 days/wk for 12 weeks). Group sizes were generally 4-6 participants. **Outcome Measure:** Attention Rating and Monitoring Scale (ARMS), Behavioural Assessment of the Dysexecutive Syndrome,	1. There was a significant treatment effect for the EF index favoring the IS group (p=0.008). 2. There was no significant difference between groups in the DERS of ARMS. 3. Secondary analysis revealed a significant treatment effects for the FeSBe scale (p=0.049) and the PSI (p=0.016). 4. There were no other significant treatment effects. Variance of depression, age, severity and time since injury did not change treatment effects.

	Difficulties in Emotion Regulation Scale (DERS), Executive Function Composite from Factor Analysis (EF index), Problem Solving Inventory (PSI), Frontal System Behavioural Scale (FrSBe).	
Vas et al. (2011) USA RCT PEDro=6 N=28	**Population:** TBI: *Strategic Memory and Reasoning Training (SMART) Group* (n=14): Mean Age=39 yr; Gender: Male=9, Female=5; Mean Time Post Injury=16.71 yr. *Brain Health Workshop Group* (n=14): Mean Age=47 yr; Gender: Male=7, Female=7; Mean Time Post Injury=16.35 yr. **Intervention:** Participants were randomly assigned to the SMART group or the BHW group. Participants received a total of 12 group sessions over an 8 wk period. The SMART group learned about strategies they could apply in their daily lives; homework was given at the end of each session. The BHW group sessions were designed to be information-based and reading assignments were given each week. Participants were assessed at baseline, post-training (3 weeks) and at a 6 month follow-up. **Outcome Measure:** Test of Strategic Learning (TOSL); Working memory listening span task; Community Integration Questionnaire (CIQ); Wechsler Adult Intelligence Scale III (WAIS III).	1. The SMART group had significantly greater TOSL scores compared to the control group post-training (SMART *Mean*=19.76, BHW *Mean*=13.69, p=0.030). 2. The SMART group had significant improvements in TOSL scores: post-training (*Mean*=19.76, p=0.007) and at 6-month follow-up (*Mean*=21.15, p=0.004) from baseline (*Mean*=14). 3. The SMART group had significantly greater improvements than the control group on the working memory listening span task post-training (SMART *Mean*=4.23, BHW *Mean*=2.59, p<0.001). 4. The SMART group had significant improvements post-training in the working memory listening span task (*Mean*=4.23, *p*=0.005) and at 6-month follow-up (*Mean*=4.96, P=0.0001) compared to baseline (*Mean*=2.76). 5. The SMART group had significantly greater improvements on CIQ compared to the BHW group (SMART *Mean*=18.73, BHW *Mean*=16.45, p=0.020). 6. The SMART group had significant improvements in the CIQ at the 6-month (*Mean*=19.88, p=0.010) follow-up from baseline (*Mean*=15.19). 7. Those in the SMART group showed significant improvement on 3 executive functions following training (inhibition: p=0.010; nonverbal reasoning: p=0.001; and cognitive flexibility: p=0.010) on the WAIS-III.
Chen et al. (2011) USA RCT PEDro=5 N=12	**Population:** TBI=9, Other=3: Mean Age=48 yr; Gender: Male=5, Female=7; Time Post-Injury Range=6 mo-6 yr. **Intervention:** Participants were randomized to receive either the goals training intervention (n=7) or education intervention (n=5) for 5 wk, after which they switched to the other condition for another 5 wk. The goals training was spread over 5 wk and involved: group, individual and home-based training. The education program was a 5 wk didactic educational instruction regarding brain injury. **Outcome Measures:** Letter number sequencing, Wechsler Adult Intelligence Scale-III, Auditory consonant trigrams, Digit Vigilance Test, Design and Verbal Fluency Switching, Trails B, Stroop Inhibition, Hopkins Verbal Learning Test, Brief Visual Memory Test Revised, Trails A test, Visual Attention Task.	1. On the domain of attention and executive functions, all participants in the goal training intervention showed an increase from pre to post goals training; while only 7/12 in the education intervention showed an increase from pre to post education (p<0.0001). 2. For learning and memory performance scores increased an average of 0.70 units after participation in goals training than after participation in education intervention (p=0.020). 11/12 participants improved in the goals training group while 4/12 improved in the education group (p=0.009). 3. Tests of motor speed of processing showed no significant differences between the two interventions with a

		non-significant trend for greater improvements in goal-training compared to education (p=0.070).
Novakovic-Agopian et al. (2011) USA RCT Crossover PEDro=5 N=16	**Population:** TBI=11, Stroke=3, Other=2: Mean Age=50.4 yr; Gender: Male=7, Female=9; Time Post Injury Range=1-23 yr. **Intervention:** Participants were randomized to 5 wk interventions consisting of a goals training program (n=8) or an educational instruction group (n=8). Goal training focused on mindfulness-based attentional regulation and goal management strategies for participant-defined goals. Educational training was didactic instructional sessions about brain injury. At the end of 5 wk, participants were switched to the other intervention. All participants were assessed at baseline, Week 5 and again at Week 10. **Outcome Measure:** Auditory Consonant Trigrams, Letter Number Sequencing (working memory); Digit Vigilance Test (sustained attention); Stroop Inhibition Delis-Kaplan Executive Function System (Inhibition); Trails B, Design Fluency-switching (mental flexibility), Hopkins Verbal Learning Test-Revised, Brief Visual Memory Test-Revised.	1. At the end of wk 5 participants in the goals-edu group showed significant improvement on measures of attention and executive function from baseline (p<0.0001), while the edu-goals group showed no change or minimal change (p>0.050). 2. The goals-edu group had significantly greater improvements than the edu-goals group on the following at wk 5: working memory (M*ean* 1.12 vs -0.12, p<0.0001); mental flexibility (*Mean* 0.64 vs 0.04, p=0.009); inhibition (*Mean* 0.62 vs 0.04, p=0.005); sustained attention (*Mean* 0.96 vs 0.27, p=0.010); learning (*Mean*=0.51 vs 0.08, p=0.020); and delayed recall (*Mean* 0.39 vs -0.27, p=0.010). 3. At wk 10, the edu-goals group significantly improved compared to wk 5 on: attention and executive function (0.79 vs 0.03, p<0.0001); working memory (1.31 vs -0.12, p<0.0008); mental flexibility (0.66 vs 0.04, p<0.0008); inhibition (0.50 vs 0.04, p=0.010); sustained attention (0.44 vs 0.27, p=0.010); memory (0.609 vs -0.10, p=0.020); learning (0.66 vs 0.08, p=0.050); and delayed recall (0.55 vs -0.27, p=0.020). 4. Those in the goals-edu group who had completed the training session were able to maintain their gains and there were significant improvements in attention and executive function (p<0.040) and working memory (p<0.020).
Ownsworth et al. (2008) Australia RCT PEDro=9 N=35	**Population:** TBI=21, Other=14; Mean Age=43.89yr; Gender: Male=19, Female=16; Mean Time Post Injury=5.29yr. **Treatment:** Participants were randomized to receive one of three 8wk intervention groups for goal attainment: individual (n=10), group (n=11), or combined (n=10). Individual treatment occurred in participant homes and community while also focusing on client-centered goals. Group-based treatment involved education, peer and facilitator feedback, and goal setting. The combined group received the equivalent amount of individual and group therapy. **Outcome Measure:** Canadian Occupational Performance Measure (COPM): performance self-rating, satisfaction self-ratings, relatives'	1. There were significant improvements on performance self-ratings between pre-post intervention for the individual (4.08 to 6.78, p<0.01) and combined interventions (5.04 to 6.98, p<0.01) but not the group intervention (4.68 to 6.10, p=0.029). At follow-up, all interventions had significant improvements from pre-intervention (p<0.01). 2. There were significant improvements on the satisfaction self-ratings between pre-postintervention for all three interventions: individual (3.75 to 7.22, p<0.001), group (4.51 to 5.95, p<0.025) and combined (4.35 to 7.47, p<0.01). 3. There were significant improvements for relatives' rating of performance between pre-post intervention for the

	performance ratings, and relatives' satisfaction ratings.	individual (3.94 to 6.53, p<0.01) and combined interventions (4.37 to 5.32, p<0.025) but not the group intervention (4.78 to 5.93, p=0.028). At follow-up, all interventions had significant improvements (p<0.01).
Rath et al. (2003) USA RCT PEDro=2 N=46	**Population:** TBI: Mean Age=43.6 yr; Gender: Male=23, Female=37; Mean Time Post Injury=48.2 mo. **Intervention:** Patients were randomized into the innovative (n=32) or conventional (n=28) treatment groups. The innovative group received 24, 2 hr sessions focusing on emotional self-regulation and clear thinking. The conventional group received 24, 2-3 hr sessions focusing on cognitive remediation and psychosocial groups. **Outcome Measure:** Weinberg Visual Cancellation Test, Stroop Color–Word Task, FAS—Controlled Oral Word Association Test, Will-Temperament Scale, Visual Reproduction, Immediate and Delayed recall, Watson-Glaser Critical Thinking Appraisal, Wechsler Adult Intelligence Scale—III.	1. The innovative group showed significant improvements in visual memory immediate recall (p<0.001). 2. The conventional and the innovative group showed significant improvements: on logical memory recall (p<0.001), logical memory delayed recall (p=0.010), and visual memory delayed recall (p=0.010). 3. The conventional group had significant improvements in reasoning (p<0.050). 4. The innovative group had significant improvements in executive function (p<0.050); problem-solving self-appraisal (p=0.005); self-appraised clear thinking and emotional self-regulation (p<0.010); and observer ratings of roleplayed scenarios (p<0.005).
Copley et al. (2015) Australia Pre-Post N=8	**Population:** ABI; Mean Age=44.5 yr; Gender: Male=5, Female=3; Mean Time Post Injury=12 mo; Severity: Moderate-Severe. **Intervention:** All participants completed a treatment consisting of metacognitive strategy instruction (MSI) during 3 components. 1) Individualized sessions (IS) consisted of identifying language based goals and strategies to accomplish them (2 hr x2 sessions). 2) Group sessions (GS) where participants work on their goals in a group setting completing auditory and written comprehension tasks (1.5 hrs). 3) Daily home practice sessions (HS) involved transferring the skills learnt in the first 2 components into everyday life by teaching the significant other how to implement MSI. **Outcome Measure:** Measure of Cognitive-Linguistic Abilities Subtests: Paragraph Comprehension, Story Recall, Verbal Abstract Reasoning, Functional Reading, Factual Comprehension, Inferential Reasoning Skills (Low Level and High Level).	1. There was no significant difference in pre-post scores for paragraph comprehension (p=0.340). 2. There was no significant difference in pre-post scores for story recall (p=0.028). 3. There was no significant difference in pre-post scores for verbal abstract reasoning (p=0.111). 4. There was no significant difference in pre-post scores for functional reading (p=0.204). 5. There was no significant difference in pre-post scores for factual comprehension (p=0.891). 6. There was no significant difference in pre-post scores for inferential reasoning skills, both low level (p=0.125) and high level (p=0.020).
Gabbatore et al. (2015b) Italy Pre-Post $N_{Initial}$=20, N_{Final}=15	**Population:** TBI; Mean Age=36.7 yr; Gender: Male=10, Female=5; Mean Time Post Injury=76.1 mo; Mean GCS=4.5. **Intervention:** Participants completed a cognitive group rehabilitation program focussed on mental representations underlying one's behaviours (2 x/week for 3 months). Each session consisted of comprehension activities (discussing specific communication modalities) and production activities (role-playing activities). Participants	1. No significant improvements in ABaCo (production and comprehension) were observed from T0 to T1. 2. Participants showed significant improvements from T1 to T2 for ABaCo comprehension (p<0.001), production (p<0.001), linguistic (p=0.005), extralinguistic (p=0.008), paralinguistic (p=0.02), and context (p=0.01). 3. The improvements made during the treatment period were stable between

	were assessed at T0 (3 months before intervention (regular activities during this time), T1 (before intervention), T2 (after intervention) and T3 (3 month follow-up – regular activities during this time). Total study duration was 9 months. **Outcome Measure:** : Assessment Battery for Communication (ABaCo-comprehension, production, linguistic, extralinguistic, paralinguistic, and context), Verbal Span Task (VST), Spatial Span Task (SST), Attentive Matrices Test (AMT), Trail Making Test (TMT), Tower of London Test (TOL), Colored Progressive Matrices Raven (CPM Raven), Aachener Aphasie Test-Denomination Scale (AAT), Sally-Ann Task, Strange Stories Task, Immediate and Deferred Recall Test (IDR), Wisconsin Card Sorting Test (WCST).	T2 and T3 for both Comprehension (p=0.86) and Production (p=0.32). At T3, AbaCo scores did not show significant differences from T2. 4. There was no significant difference between T1 and T2 on the VST (p=0.49), SST (p=0.74), AMT (p=0.35), TMT (p=0.45), TOL (p=0.50), CPM Raven (p=0.09), AAT (p=0.22), Sally-Ann (p=0.58), or strange stories task (p=1.00). 5. There was a significant improvement between T1 and T2 on the IDR (p=0.01) and WCST (p=0.003).
Llorens et al. (2012) Spain Pre-Post N=10	**Population:** ABI=10; Mean Age=41.1yr; Gender: Male=7, Female=3; Mean Time Post Injury=402.2d. **Intervention:** Participants underwent sessions (1hr/wk for 8mo) using an interactive touch screen based game asking questions related to knowledge, reasoning, action, and cohesion in groups of ≤4. Testing of participants occurred at baseline and post intervention. **Outcome Measure:** Self-Awareness Deficits Interview (SADI), Social Skills Scale (SSS).	1. On the SADI, after treatment all participants perceived their deficits properly compared to only 4 participants at baseline; 2 participants had difficulty perceiving their disability post treatment compared to 7 participants at baseline and 5 participants had difficulty establishing realistic goals post treatment compared to 7 at baseline. 2. On the SSS at baseline, 6 participants showed altered levels in social skills, compared to 2 following treatment.
Parente & Stapleton (1999) USA Case-Control N=33	**Population:** ABI. **Intervention:** A one year measure of group cognitive skills (CSG) training module. **Outcome Measure:** Return to work.	3. Ten of 13 CSG clients who completed the training program by the end of the year had maintained full employment for >60 days (76%) - versus 58% of the control group. Significance not calculated.

PEDro = Physiotherapy Evidence Database rating scale score (Moseley et al., 2002a).

Discussion

Several studies have evaluated the effects of group goal management training. One study has compared the effect of group Goal Management Training (TG) to a group Brain Health workshop (CG) on cognitive outcomes post brain injury (Tornas et al. 2016). The study showed that individuals receiving goal management training improved significantly in cognitive and executive outcomes after treatment, and at 6-month follow-up. While this study showed promising results, it is important to remember that despite its rigorous methodology, the patient population was very heterogenous and it is unclear how different injuries impacted the outcomes. Similar results of goal management training were found in an RCT by Novakovic-Agopian et al. (2011), where a goals training group showed significant improvement on attention and executive function assessments compared to the educational group. Despite switching interventions at the 5-week mark to the educational intervention, the goal training group continued to improve significantly. Interestingly, an RCT published in the same year also demonstrated that goal training is beneficial for executive functions (Chen et al., 2011). In this study both groups significantly improved in attention directed goal completion. A final RCT evaluated group goal attainment interventions compared to educational interventions (Ownsworth et al., 2008). This study found that all individuals who received goal attainment interventions significantly improved over time on measures of executive functioning, regardless of group assignment at 3-month follow-up based on self-ratings, and relative's ratings (Ownsworth et al., 2008).

Emotional regulation was also examined as a potential intervention for the remediation of attention and executive dysfunction post ABI (Cantor et al., 2014; Rath et al., 2003). While this treatment was not found to be effective in the recovery of attention, significant improvements on executive function were noted (EF, FeSBe, PSI) (Cantor et al., 2014). Further support for emotional oriented intervention can be found in an earlier study by Rath et al. (2003). The group completed an RCT comparing two cognitive rehabilitation therapies: conventional (cognitive remediation and psychosocial components) versus an innovative rehabilitation approach focusing on emotional self-regulation and clear thinking. Outcomes were measured across multiple domains of cognition including attention, memory, reasoning, psychosocial functioning, and problem-solving measures. Significant changes comparing baseline to post intervention outcomes were seen for each group on problem-solving measures; however, the improvements were different for the interventions. No between-group comparisons were made.

A pre-post study by Copley et al. (2015) investigated the effects of a Metacognitive Strategy Instruction (MSI) intervention on verbal and cognitive outcomes post ABI. The program was delivered individually, in a group-setting, and at home. Despite the multi-step process, no improvements were observed in cognitive or verbal abilities from baseline after the intervention. Gabbatore et al. (2015) implemented a cognitive group rehabilitation program for patients post TBI, and discovered that compared to before the intervention, patient's recall (IDR), attention (WCST), and communication skills (ABaCo) all significantly improved. Specifically, the ABaCo was used to measure linguistic comprehension and context comprehension.

In addition to its use as a memory intervention the Strategic Memory and Reasoning Training (SMART) program is also an effective intervention for executive functioning. Vas et al. (2001) compared its use to that of a brain health workshop. The SMART group had significantly higher scores on the Test of Strategic Learning, and Wechsler Adult Intelligence Scale III for sections examining inhibition, non-verbal reasoning, and cognitive flexibility, demonstrating an overall improvement in metacognition and comprehension.

Only one study using a technology-based intervention met our inclusion criteria. Llorens et al. (2012) used an interactive touch screen game in an attempt to improve social skills and self-awareness following ABI. Although no formal statistical analysis took place, at the end of the treatment period all participants had an accurate perception of their deficits (compared to 4/10 at baseline), and six of ten participants showed alterations in their social skills (Llorens et al., 2012).

Parente and Stapleton (1999) compared brain injury survivors who completed a cognitive skills group to comparable controls. The cognitive skills group interventions included education regarding "thinking skills" such as problem solving, concentration/ attention, decision making, remembering names and faces, study skills, functional mnemonics, prosthetic memory devices, social cognition, organizational skills and goal setting. Other important aspects of the cognitive skills group included computer training, prosthetic aid training, interviewing skills training and focus on a model of clients teaching clients. There was no statistical analysis completed; however, the return to work rate for 13 of 33 participants assigned to the cognitive skills group training was 76% as compared to 58% for the control group. Competitive employment for the intervention group was maintained at 6-month follow up.

Conclusions

There is level 1b evidence that goal orientated group interventions are successful at improving cognitive and executive function in patients post ABI.

There is level 1b evidence that emotional regulation group interventions are effective at improving executive function in post TBI patientscompared to standard therapy.

There is level 1b evidence that the Strategic Memory and Reasoning Training program is more effective than a brain health workshop for improving executive function, metacognition, and comprehension following ABI.

There is level 4 evidence that metacognitive strategy instruction may not be effective for improving executive functioning following an ABI.

There is level 4 evidence that touch screen-based games (which include components of reasoning and problem-solving) may be effective for improving self-awareness and social skills following an ABI.

Group goal-oriented interventions are effective for the remediation of executive functions, including comprehension and problem solving.

Emotional regulation interventions delivered in a group setting may improve executive function in patients post TBI; however, it is unclear if it is superior at doing so compared to conventional cognitive remediation.

The SMART program appears to be effective for improving executive functioning following an ABI.

Touch screen-based games which include components of metacognition may be effective for improving self-awareness.

Metacognitive instruction does not appear to improve comprehension or abstract reasoning; however, more studies are needed to fully evaluate its effects.

6.3.1.2 Rehabilitation of General Cognitive Functioning

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

Gordon et al. (2006) conducted an extensive review of the TBI rehabilitation literature and identified 13 studies examining treatments for cognitive deficits. Studies included in that review had a multitude of inclusion criteria. Additionally, the studies identified were of limited methodological quality, but suggested that compensatory strategy training improved attention deficits and mild memory impairments (Gordon et al., 2006). Several researchers have noted that training-based therapies that target executive control, such as "*attention, problem solving, and the use of metacognitive strategies*" (Novakovic-Agopian et al., 2011) may improve functioning in those who sustain an ABI (Cicerone, 2002; Kennedy et al., 2008a;

Sohlberg et al., 2003b). Studies included in this section have examined the effects of cognitive rehabilitation strategies.

Table 6.33 The Effect of Cognitive Rehabilitation Strategies on General Cognitive Function Post ABI

Author Year Country Research Design PEDro Sample Size	Methods	Outcome
Linton & Kim (Linton & Kim, 2018) (2018) United States RCT PEDro=5 N=8	**Population:** Mean age=36.5yr; Gender: Male=4, Female=4. **Intervention:** Participants were either assigned to the 3-month, in home, Trabajadora de Salud group or the control group. The control group received the same intervention only via telephone. **Outcomes:** Neurobehavioral Functioning Inventory, Physical FIM, Cognitive FIM.	1. Both the experimental and control groups saw a decrease in their depressive symptoms on the Neurobehavioral Functioning Inventory. 2. Both groups saw an increase in physical FIM scores, although the experimental groups was slightly higher. 3. Only the experimental group saw an increase in Cognitive FIM scores. 4. No between-subjects' analyses were performed.
Schmidt et al. (2013)(Schmidt et al., 2013) Australia RCT PEDro=8 N=54	**Population:** *Video Feedback (N=18)*: Mean age=42.7yr; Gender: Male=14, Female=4; Mean time post-injury=1.5yr; Mean GCS=8.1. *Verbal Feedback (N=18):* Mean age=41.6yr; Gender: Male=14, Female=4; Mean time post-injury=4.7yr; Mean GCS=7.1. *Experimental Feedback (N=18):* Mean age=37.5yr; Gender: Male=18; Mean time post-injury=5.8yr; Mean GCS=7.0. **Intervention:** Participants received instructions for meal preparation on 4 occasions in one of three formats. The video feedback group watched their recorded meal preparation sessions, the verbal feedback group received feedback on task completion without the video, and the experimental group received no therapist feedback on task completion. **Outcomes:** Error rate, Awareness Questionnaire (AQ), Depression Anxiety Stress Scales (DASS-21), Self-perceptions in Rehabilitation Questionnaire (SPIRQ).	1. There were significant differences between groups at baseline on measures of functional independence ($p<0.01$), and logical memory ($p<0.05$). 2. The video feedback group significantly improved online awareness more than either of the other two groups ($p<0.001$), and also had significantly fewer errors than either group ($p<0.05$). 3. The video feedback group had significantly higher intellectual awareness on the AQ ($p<0.05$). 4. There were no significant differences between groups on the DASS-21 or the SPIRQ.
Goverover et al. (2007) United States RCT PEDro=6 N=20	**Population:** *Experimental Group (N=10)*: Mean age=39.5yr; Gender: Male=8, Female=2; Mean time post-injury=12.9mo; Mean GCS=4.6. *Control Group (N=10)*: Mean age=39.2yr; Gender: Male=8, Female=2; Mean time post-injury=8.6mo; Mean GCS=3.6. **Intervention:** Six individualized cognitive treatment task sessions were administered over three weeks, with one session per day 2-3 days a week. Tasks included everyday activities such as making lunch, or a telephone call. **Outcomes:** Assessment of awareness of disability (AAD), Assessment of Motor and Process Skills (AMPS), Activities of Daily Living (ADL), Relf-Regulation Skills Interview (SRSI), Satisfaction with quality of care, Awareness Questionnaire (AQ), Community Integration Questionnaire (CIQ).	1. Groups were not statistically different at baseline. 2. There were no significant differences between groups following treatment on AAD. 3. There was a significant improvement in the experimental group on SRSI scores compared to the control group ($p<0.05$). 4. There was a significant improvement in AMPS and ADLs for the experimental group, compared to the control group ($p<0.05$, $p<0.05$), only on measures of processing and cognition. There were no significant differences on measures of motor AMPS or motor ADLs. 5. There were no significant differences between groups on AQ or CIQ.

Author Year Country Research Design PEDro Sample Size	Methods	Outcome
Neistadt et al. (1992) USA RCT PEDro=6 N=45	**Population:** TBI: Mean Age=33.2 yr; Gender=Male; Time since injury=7.9 yr. **Intervention:** Participants were randomly assigned to an adaptive (n=23) or a remedial (n=22) approaches for their occupational therapy. **Outcome Measure:** The Parquetry Block test; Block design subtest of the Wechsler Adult Intelligence Scale-Revised (WAIS-R).	1. After treatment, the remedial group improved significantly more than the adaptive group on the Parquetry Block test (p=0.019), but there were no significant differences on the WAIS-R Block Design subtest. 2. There was a non-significant tendency in the expected direction to support that the adaptive group would perform better than the remedial group on the RKE-R after treatment.
Combs et al. (Combs et al., 2018) United States Pre-Post N=19	**Population:** Mean age=32.8yr; Gender: Male=89.5%, Female=10.5%; TBI injury severity: mild=15.8%, severe=63.2%, Other=21.1%. **Intervention:** All individuals experienced weekly group meetings around topics in mindfulness-based stress reduction. Each group session lasted 60 mins and group sessions were completed over the course of 32 weeks. **Outcomes:** Participants were asked dichotomous questions, or on a Likert-scale about their psychological wellbeing, cognitive functioning, and physical health and their beliefs of the efficacy of the intervention related to those topics.	1. Overall, the majority of participants reported a significant improvement in their overall health (p<0.001) in relation to the number of sessions they attended. 2. Participants also reported their beliefs in the ability of the number of sessions to improve physical health symptoms (p<0.05), focus and attention (p<0.05), self-awareness (p<0.05), and mood and anxiety (p<0.001). 3. No similar significant relationship was found for measures on sleep benefits, or pain.
Rasquin et al. (2010) Netherlands Cohort N=52	**Population:** Mean Age: 49.5 yr; Gender: male=14, female=13; Mean Time Post-Injury:1.9 yr; Condition: CVA=9, TBI=5, Other ABI=13. Controls who were relatives of the patients=25. **Intervention:** Participants were asked to formulate individual strategies to address specific cognitive issues (attention memory or problem solving) and to develop methods to ask for help with problems resulting from the head injury. Caregivers were asked to attend sessions. Sessions lasted approximately 2.5 hours and ran for approximately 15 weeks. Assessment was conducted at baseline, 21 weeks after treatment, 6 months after treatment. **Outcome Measure:** Goal Attainment Scaling; Stroke Adapted Impact Scale; Cognitive Failure Questionnaire	1. Results from the Goal Attainment Scaling, the Stroke Adapted Impact Scale and the Cognitive Failure Questionnaire all indicate there was significant improvement from baseline (T0) to immediately after treatment (T1) (p<0.05). 2. Patients improved on significantly on individual goals (p<0.05) between T0 to T1. 3. No further changes were noted on the primary outcomes 6 months post intervention (T2).
Laatsch et al. (1999) USA Case series N=5	**Population:** TBI; Age Range=18-65yr; Time Post-Injury=2-48 months; **Intervention:** Cognitive rehabilitation therapy (CRT) programme in a longitudinal protocol involving a resting SPECT and neuropsychological evaluation are pre-treatment, post-treatment and post non-treatment intervals. **Outcome Measure:** Neuropsychological measures.	1. NP measures: WAIS-R, WMS-R, CVLT, RCFT, SCWT, WCST or ACT, SPECT image. 2. SPECT data revealed significant increases in cerebral blood flow during the treatment period (p<0.05). 3. CRT was found to be effective in improving both NP and everyday functioning. All patients were able to be more productive in their lives following treatment.

PEDro = Physiotherapy Evidence Database rating scale score (Moseley et al., 2002a)

Discussion

Seven studies investigating the remediation of general cognitive functioning were found meeting our inclusion criteria. Neistadt (1992) divided 45 patients into one of two groups: a remedial group who received individual training with parquetry block assembly, and an adaptive group who received functional skills training over a six-week period. Outcomes for the effect of treatment for constructional test performance revealed that the remedial group improved significantly more than the adaptive group on the Parquetry Block test. However, there were no significant differences on the WAIS-R Block Design subtest after treatment. Training-specific learning appears to be an effective approach to rehabilitation as demonstrated by the treatment effect.

Goverover et al. (2007) used an RCT to study individualized cognitive treatments (such as making lunch or a telephone call) on the ability to remediate self-awareness and generalized processing skills. Groups did not significantly differ at baseline; however, following treatment individuals in the treatment group experienced a significant increase in their self-regulation, and processing skills (Goverover et al., 2007). In a study, Rasquin and colleagues (2010) they investigated the effectiveness of a low intensity outpatient cognitive rehab program on those (n=27) who had sustained an ABI. All participants were in the chronic phase of recovery and all were asked to invite a caregiver to attend sessions with them (n=25). Sessions lasted 2.5 hours each week for a total of 15 weeks. All were assessed prior to the session beginning, immediately afterward and again 6 months later. Participants worked on developing strategies to assist them with their attention, memory and problem-solving difficulties. Social skills training sessions were also held. Changes were noted immediately after the cognitive rehab program ended and this improvement in goal attainment, and cognitive improvement was maintained at the 6-month follow-up. Laatsch et al. (1999) found similar results where cognitive rehabilitation therapy helped individuals increase productivity in their daily lives and found improvements on neuropsychological measures.

Two other RCTs have evaluated specific training programs attempting to improve generalized cognitive functioning (Linton & Kim, 2018) (Schmidt et al., 2013). The more recent RCT had individuals participate in the in-home program (Trabajadora de Salud) and found that although both groups improved on physical measures over time, only the experimental group saw a significant increase in cognitive FIM scores. The second study involved individuals receiving task completion instructions in a variety of formats to determine how feedback might influence general cognition (Schmidt et al., 2013). Those in the video feedback group (compared to verbal feedback) saw significant improvements in self-perception, and general awareness. The video feedback condition showed a recording of the individual performing the meal preparation task required with corrective feedback, compared to the verbal feedback group which only received verbal corrective feedback (Schmidt et al., 2013).

Mindfulness-based stress reduction was evaluated in an attempt to improve self-awareness and overall cognitive health (Combs et al., 2018). Individuals participated in weekly mindfulness sessions for 60 minutes and were asked to self-report on their general cognitive functioning. Individuals reported a significant reduction in cognitive symptoms which was positively correlated to the number of sessions they attended. This was true for both general cognitive functioning as well psychological wellbeing. Although this single pre-post study offers insight into the benefits of mindfulness-based stress reduction, more research is needed.

Conclusions

There is level 1b evidence that cognitive therapies compared to standard therapy are more effective than no therapy for improving generalized cognitive functioning, as well as self-perception following an ABI.

There is level 4 evidence that a low intensity outpatient cognitive rehabilitation program may improve goal attainment and cognitive impairment in patients post ABI.

There is level 2 evidence that the Trabajadora de Salud program may improve general cognitive functioning compared to standard therapy for those with an ABI.

There is level 1b evidence that corrective video feedback is more effective for improving generalized cognitive functioning and self awareness compared to verbal feedback only in those with an ABI.

There is level 1b evidence that remedial occupational therapy and adaptive occupational therapy may have equal effects on generalized cognitive function in those with an ABI.

There is level 4 evidence that mindfulness-based stress reduction may be effective for improving general cognitive functioning and psychological health for those with an ABI.

General cognitive rehabilitation programs are effective for improving cognitive functioning following an ABI.

There is limited evidence that mindfulness based stress reduction is effective for improving cognitive functioning.

Corrective video feedback is more effective than verbal feedback alone for improving general cognitive function and self-awareness.

Remedial and adaptive occupational therapy are equally effective for improving general cognitive functioning.

6.3.2 Pharmacological Interventions

6.3.2.1 Donepezil

The effectiveness of donepezil, a cholinesterase inhibitor, in improving cognitive and memory functions following brain injury was assessed. Cognitive impairments negatively impact patient autonomy, affecting one's ability to return to work or school, and live alone (Masanic et al., 2001). When tested in individuals diagnosed with Alzheimer's disease, donepezil has been found to be useful in treating memory problems (Morey et al., 2003; Walker et al., 2004). The impact of Donepezil impact on cognitive function and memory in a TBI population is explored in the table below.

Table 6.34 The Effect of Donepezil on Executive and General Cognitive Functioning Post ABI

Author Year Country Research Design PEDro Sample Size	Methods	Outcome
Khateb et al. (2005) Switzerland Pre-Post $N_{initial}$=15, N_{final}=10	**Population:** TBI; Mean age=43 yr; Gender: Male=8, Female=7; Mean Time Post Injury=4 2mo. **Intervention:** Patients were administered donepezil 5 mg/day for 1 mo, followed by 10 mg/day for 2 mos. **Outcome Measure:** Stroop test, Trail Making Test (TMT), Rey Auditory Verbal Memory Test (RAVMT), Test for Attentional Performance (TAP).	1. Four of 15 participants stopped due to side effects within the first week (e.g., nausea, sleep disorders, anxiety, dizziness, etc.). 2. Changes on the neuropsychological evaluation show modest improvement. However, the comparison of the global score of all questionnaires before and after therapy was not significant (p=0.058). 3. A significant improvement in executive function was only found for the Stroop Colour naming test (87.3±22.9 to 79.5±19.1, p=0.030); the RAVMT-learning for learning and memory (47.7±6.9 to 53.5±5.0, p=0.050); and the errors subsection of divided attention for attention, (5.8±3.3 to 2.9±2.7, p=0.030).

Discussion

Khateb et al. (2005) found only modest improvement on the various neuropsychological tests used to measure executive function, attention, and learning and memory. Of note, results from the learning phase of the Rey Auditory Verbal Memory Test (RAVMT) showed significant improvement (p<0.050). The Donepezil intervention also demonstrated improvement in executive function, as the results from the Stroop-colour naming test showed significant improvements (p<0.030). On the test for Attentional Performance a significant change was noted on the divided attention (errors) subsection of the test. Overall, donepezil was found to be effective in improving learning, memory, divided attention, and executive function. However, possible benefits of donepezil administration must be balanced against the observed side effects in 27% of the population. Further randomized control trials are required to better explore the efficacy of donepezil post TBI.

Conclusions

There is level 4 evidence that donepezil is effective in improving learning, memory, divided attention, and executive function in patients post TBI.

Donepezil might improve attention, learning and short-term memory following TBI; however, side effects may incur from its use.

6.3.2.2 Methylphenidate

Methylphenidate is a stimulant which inhibits the reuptake of dopamine and norepinephrine and increases activity in the prefrontal cortex. In the past, methylphenidate has been extensively used as a treatment for attention deficit disorder, as well as narcolepsy (Glenn, 1998). A total of three RCTs examined the efficacy of methylphenidate as a treatment for the recovery of executive and general cognitive deficits post ABI.

Table 6.35 The Effect of Methylphenidate on Executive and General Cognitive Functioning Post ABI

Author Year **Country** **Research Design** **PEDro** **Sample Size**	**Methods**	**Outcome**
Dymowski et al. (Dymowski et al., 2017) Australia RCT PEDro=9 $N_{Initial}$=11, N_{Final}=10	**Population:** TBI. *Methylphenidate Group (n=6)*: Mean Age=35 yr; Gender: Male=4, Female=2; Mean Time Post Injury=366 d; Mean Worst GCS=4.83. *Placebo Group (n=4)*: Mean Age=32.5 yr; Gender: Male=2, Female=2; Mean Time Post Injury=183.5 d; Mean Worst GCS=4.50. **Treatment:** Participants were randomly assigned to receive either methylphenidate (0.6 mg/kg/d rounded to the nearest 5mg with maximum daily dose of 60 mg) or placebo (lactose). Outcomes relating to processing speed, complex attentional functioning, and everyday attentional behaviour were assessed at baseline, 7 wk (on-drug), 8 wk (off-drug), and 9 mo follow-up. **Outcome Measure:** Symbol Digit Modalities Test (SDMT), Trail Making Test (TMT) A and B; Hayling (A, B, error), Digit Span (DS-Forward, Backward, Sequencing, Total), Ruff 2&7 Selective Attention Test Automatic Speed Raw Score (2&7 ASRS), Ruff 2&7 Selective Attention Test Controlled Speed Raw Score (2&7 CSRS), Simple Selective Attention Task Reaction Time (SSAT RT), Complex Selective Attention Task Reaction Time (CSAT RT), N-back 0-back RT, N-back 1-back RT, N-back 2-back RT, Rating Scale of Attentional Behaviour Significant Other (RSAB SO).	1. After applying Bonferroni corrections, no significant differences between groups from baseline to 7 wk, baseline to 8 wk, or baseline to 9 mo were observed for SDMT, TMT A, TMT B, Hayling A, Hayling B, Hayling error, DS Forward, DS Backward, DS Sequencing, DS Total, 2&7 ASRS, 2&7 CSRS, SSAT RT, CSAT RT, N-back 0-back RT, N-back 1-back RT, N-back 2-back RT, or RSAB SO.
Zhang and Wang (Zhang & Wang, 2017) China RCT PEDro=10 $N_{Initial}$=36, N_{Final}=33	**Population:** TBI; Severity: mild to moderate. *Methylphenidate Group (n=18)*: Mean Age=36.3 yr; Gender: Male=13, Female=5. *Placebo Group (n=18)*: Mean Age=34.9 yr; Gender: Male=14, Female=4. **Treatment:** Participants were randomly assigned to receive methylphenidate (flexibly titrated from 5 mg/d at the beginning, then gradually increased by 2.5 mg/d until reaching 20 mg/d) or placebo for 30 wk. **Outcome Measure:** Mental Fatigue Scale (MFS), Choice Reaction Time (CRT), Compensatory Tracking Task (CTT), Mental Arithmetic Test (MAT), Digit Symbol Substitution Test (DSST), Mini-Mental State Examination (MMSE), Beck Depression Inventory (BDI), Hamilton Rating Scale for Depression (HAMD).	1. At baseline, there were no significant differences between groups in terms of demographics, MFS, CRT, CTT, MAT, DSST, MMSE, BDI, or HAMD. 2. Post-intervention, the experimental group had significantly lower scores compared to control group for MFS (p=0.005), CRT (p<0.001), CTT (p<0.001), BDI (p=0.040), and HAMD (p=0.005). 3. Post-intervention, the experimental group had significantly higher scores compared to control group for MAT (p=0.020), DSST (p<0.001), MMSE (p<0.001).
Speech et al. (1993) USA RCT PEDro=7 N=12	**Population:** TBI; Mean Age=27.6 yr; Gender: Male=5, Female=7; Mean Time Post Injury=48.5 mo. **Intervention:** In a crossover design, participants were randomly assigned to receive 0.3 mg/kg methylphenidate, 2×/d, for 1 wk, followed by 1wk of placebo, or receive the treatment in a reverse order. **Outcome Measure:** Gordon Diagnostic System, Digit Symbol and Digit Span subtests of the Wechsler Adult Intelligence Scale-Revised, Stroop Interference Task,	1. No significant differences were found between methylphenidate and placebo condition in any of the outcome measures studied.

Author Year Country Research Design PEDro Sample Size	Methods	Outcome
	Sternberg High Speed Scanning Task, Selective Reminding Test, Serial Digit Test, and Katz Adjustment Scale.	

PEDro=Physiotherapy Evidence Database rating scale score (Moseley et al., 2002a).

Discussion

Dymowski et al. (2017) investigated the effects of short-term, 7-week, methylphenidate administration in post TBI patientscompared to a placebo control group. There was no significant improvement, or difference between groups for various measures and tests of attention and cognition. Speech et al. (1993) conducted a double blind placebo controlled trial evaluating the effects of methylphenidate following closed head injury and arrived at similar conclusions, as the treatment and placebo group did not vary in any measurements of memory, intelligence, or attention. Conversely, Zhang and Wang (2017) used a larger sample size to investigate the effects of long-term (30 wk) methylphenidate use in patients post TBI. While there was no difference between the groups at baseline, the treatment group had improved reaction time, cognitive ability, attention capacity, and depression when compared to the placebo group. The contradictory on methylphenidate use post TBI creates an interesting conflict, as all studies were conducted with high methodological quality and proper controls. Zhang and Wang (2017) used a fraction of the dose of methylphenidate compared to the Dymowski et al. (2017) study. Although methylphenidate has been found to be effective for the management of specific cognitive functions, such as attention, its effects on general and executive function remains inconclusive.

Conclusions

There is conflicting (level 1a) evidence regarding the effectiveness of the administration of methylphenidate, compared to placebo, following TBI for the improvement of general and executive functioning.

The effectiveness of methylphenidate to improve cognitive impairment following brain injury is unclear. Further studies with larger populations are required.

6.3.2.3 Sertraline

Sertraline, better known under its trade name Zoloft (Pfizer), is a selective serotonin reuptake inhibitor (SSRI) used for the treatment of depression and mood (Khouzam et al., 2003; Jorge et al., 2016). The majority of sertraline TBI research focuses on the prevention or treatment of major depressive symptoms post brain injury. However, recent studies have shifted focus and begun to evaluate the benefits of sertraline at improving cognitive disorders (Banos et al., 2010). The study reviewed below investigated the effect of sertraline on cognitive outcomes post TBI.

Table 6.36 The Effect of Sertraline on Executive and General Cognitive Functioning Post ABI

Author Year Country Research Design PEDro Sample Size	Methods	Outcome
Banos et al. (2010) USA RCT PEDro=9 N=99	**Population:** TBI. *Treatment group (n=49)*: Gender: Male=39, Female=10; Mean Age=35.3 yr; Mean Time Post Injury=21.5 d; Mean GCS=5.8. *Placebo group (n=50):* Gender: Male=33, Female=17; Mean Age=34.5 yr; Mean Time Post Injury=19.2 d; Mean GCS=5.8. **Intervention:** Participants were randomized to either the treatment group which took sertraline daily (50 mg) or placebo. Patients were assessed at 3, 6 and 12 months. **Outcome Measure:** Wechsler Memory Index (Wechsler Adult Intelligence Scale III), Symbol-Digit Modalities Test, Logical Memory, Trial Making Test and 64-item Wisconsin Card Sorting Test.	1. More subjects in the treatment group dropped out at each time point. 2. Those in the placebo group at the 6th and 12th month assessment period were older than the control group and had higher GCS. 3. Overall, there were no significant differences between the two groups on any of the cognitive measures.

PEDro = Physiotherapy Evidence Database rating scale score (Moseley et al., 2002a).

Discussion

The effect of early administration of sertraline on cognitive functioning was evaluated by Banos et al. (2010) in an RCT. When comparing the sertraline group, who received 50 mg per day, to a control group (placebo), there were no significant between group differences on any of the neuropsychological tests. The assessments examined attention and concentration, speed of processing, memory and executive function at 3, 6 and 12 months. Cognitive functioning was not found to improve following the administration of sertraline. Of note, more patients in the sertraline group dropped out of the study compared to the control group when this was quantified at all assessment points indicating the potential side effects associated with the treatment. Combined with the lack of apparent benefit to using the drug, use of sertraline is not currently recommended.

Conclusions

There is level 1b evidence that sertraline does not improve cognitive functioning, compared to placebo, in individuals who have sustained a moderate to severe TBI.

Sertraline has not been shown to improve cognitive functioning within the first 12 months post TBI and may be associated with side effects.

6.3.2.4 Amantadine

Amantadine is a non-competitive N-methyl-D-aspartate receptor antagonist and has been used as an antiviral agent, prophylaxis for influenza A, as a treatment of neurological diseases such as Parkinson’s Disease, and for the treatment of neuroleptic side-effects such as dystonia, akinthesia and neuroleptic malignant syndrome (Schneider et al., 1999). Amantadine is also thought to interact pre- and post-synaptically (Napolitano et al., 2005). Three studies were identified that investigated the effectiveness of amantadine as a treatment for the remediation of cognitive functioning following TBI.

Table 6.37 The Effect of Amantadine on Executive and General Cognitive Functioning Post ABI

Author Year Country Research Design PEDro Sample Size	Methods	Outcome
Ghalaenovi et al. (2018) Iran RCT PEDro=10 N=40	**Population:** *Amantadine Group (N=19)*: Mean age=32.16yr; Gender: Males=19, Female=0; Mean GCS=7.1; Mean time post-injury=3.21days. *Control Group (N=21)*: Mean age=40.95yr; Gender: Male=18, Female=3; Mean GCS=6.95; Mean time post-injury=3.42days. **Intervention:** Participants either received a placebo or 100mg of amantadine twice a day for 6 weeks. Assessments were conducted at baseline, day 3 of treatment, day 7 of treatment, at 6-weeks completion of the intervention, and 6 months post initial start time. **Outcomes:** Mini-Mental State exam (MMSE), Glasgow Outcome Scale (GOS), FOUR score, Disability Rating Scale (DRS), Karnofsky Performance Scale (KPS), mean hospitalization time.	1. There were no significant differences observed on the MMSE, GOS, DRS, or KPS. It should be noted that these measures were only taken at baseline and 6-month follow-up. 2. On day 7 the amantadine group had significantly better rising GCS scores than the control group (p=0.044). No other significant differences were observed between groups.
Schneider et al. (1999) USA RCT PEDro=5 N=10	**Population:** TBI; Mean Age=31 yr; Gender: Male=7, Female=3; GCS Score Range=3-11. **Intervention:** Patients randomized to either amantadine (50-150 mg 2 x/d) or placebo for 2 wk in a crossover design with a 2 wk washout period. **Outcome Measure:** Battery of Neuropsychological tests, Neurobehavioural Rating Scale.	1. There was a general trend towards improvement in the study sample over the 6 wk. 2. There were no significant between group differences in terms of orientation (p=0.062), attention (p=0.325), memory (p=0.341), executive flexibility (p=0.732) or behaviour (p=0.737).
Kraus et al. (2005) USA Pre-Post N=22	**Population:** TBI; Mean Age=36 yr; Gender: Male=17, Female=5; Severity of Injury: Mild=6, Moderate=6, Severe=10; Mean Time Post Injury=63.2 mo. **Intervention:** Positron emission tomography (PET) scan was done and participants received amantadine (10 0mg titrated to up to 400 mg/d over 3 wk). Amantadine was administered 3×/d (200 mg at 8AM, 100 mg at 12PM, and 100mg at 4PM) for 12 wk. **Outcome Measure:** Trail Making Test Part A and B (TMT A, TMT B), Controlled Oral Word Association Test (COWAT), Digit Span, California Verbal Learning Test (CVLT), Rey Osterreith Complex Figure-Immediate (Rey Im) and Delayed (Rey De) recall.	1. Measures of executive function, as indicated by TMT B and COWAT, were significantly improved in patients following treatment with amantadine (t=-2.47; p<0.020). 2. No significant differences were found for attention (TMT A and Digit Span) or memory (CVLT, Rey Im, and Rey De). 3. Correlational analyses with PET scan results suggest that there may be a strong relationship between executive domain improvement and changes in left pre-frontal metabolism (r=0.92; p=0.010) and left medial temporal metabolism (r=0.91; p=0.010).

PEDro = Physiotherapy Evidence Database rating scale score (Moseley et al., 2002a)

Discussion

In a small sample RCT by Schneider et al. (1999) the effects of Amantadine on cognition and behaviours were assessed. In this six-week cross-over study, patients received both placebo and amantadine for 2 weeks each, with a 2-week washout period in between. No significant differences were found between groups on measures of executive or general cognitive functioning. A recent RCT reinforces these findings after finding no significant differences on measures of cognition following 6-weeks of amantadine treatment (Ghalaenovi et al, 2018). Similarly, Kraus et al. (2005) demonstrated that the administration of amantadine over a 12-week treatment period does not improve memory deficits or attention; however, significant improvements in executive functioning were observed. Given the quality and sample size of the current studies, future studies exploring the efficacy of amantadine for learning and memory are warranted.

Conclusions

There is level 1b evidence that Amantadine may not help to improve general functioning deficits in post TBI patientscompared to placebo.

Amantadine is not effective at improving generalized cognition. Its impact on executive functioning should be studied further.

6.3.2.5 Bromocriptine

Bromocriptine is a dopaminergic agonist which primarily exerts its actions through binding and activating D_2 receptors (Whyte et al., 2008). It has been suggested that dopamine is an important neurotransmitter for prefrontal function, an important area of the brain that contributes to cognitive function, memory, intelligence, language, and visual interpretation (McDowell et al., 1998; Siddiqui et al., 2008). In a study looking at the effects of bromocriptine on rats, Kline et al. (2002) noted that the animals showed improvement in working memory and spatial learning; however, this improvement was not seen in motor abilities. Two studies have been identified investigating the use of bromocriptine as an adequate treatment for the recovery of cognitive impairments following TBI.

Table 6.38 The Effect of Bromocriptine on Executive and General Cognitive Functioning Post ABI

Author Year Country Research Design PEDro Sample Size	Methods	Outcome
McDowell et al. (1998) USA RCT PEDro=4 N=24	**Population:** TBI; Median Age=32.5 yr; Gender: Male=20, Female=4; GCS Range=3-8; Time Post injury Range=27 d-300 mo. **Intervention:** In a crossover design, participants were randomly assigned to receive bromocriptine (2.5 mg) then placebo or receive treatment in the reverse order. **Outcome Measure:** Dual-task Paradigm (counting and digit span), Stroop Test, Spatial Delayed-response Task, Wisconsin Card Sorting Test (WCST), Reading Span Test, Trail Making Test (TMT), Controlled Oral Word	1. Following bromocriptine treatment there were significant improvements on the dual-task counting (p=0.028), dual-task digit span (p=0.016), TMT (p=0.013), Stroop Test (p=0.050), COWAT (p=0.020), and WCST (p=0.041). 2. Bromocriptine had no significant effects on working memory (e.g. spatial delayed-response task and reading span test; p=0.978), or on control tasks (p=0.095).

Author Year Country Research Design PEDro Sample Size	Methods	Outcome
	Association Test (COWAT), and Control Tasks.	
Powell et al. (1996) UK Case Series N=11	**Population:** TBI=8, SAH=3; Mean Age=36 yr; Gender: Male=6, Female=5; Time Post Injury Range=2mo-5 yr. **Intervention:** Patients received bromocriptine (a maximum dose of 5-10 mg/d). Patient assessments included two baseline evaluations (BL1 and BL2), evaluation when stabilized at maximum bromocriptine dose (MAXBROMO), and two post withdrawal evaluations (POST1 and POST2). **Outcome Measure:** Percentage Participation index (PPI), Spontaneity, Motivation, Card Arranging Reward Responsivity Objective Test (CARROT), Digit Span, Buschke Selective Reminding Test (BSRT), Verbal Fluency, Hospital Anxiety and Depression Scale.	1. Reported PPI ($p<0.0001$), motivation, and spontaneity (both $p<0.005$) increased significantly from BL2 to MAXBROMO. Improvements were seen in CARROT as well ($p<0.0001$). 2. Significant improvements were observed from BL2 to MAXBROMO on the digit span ($p<0.001$), BSRT ($p<0.01$), and verbal fluency ($p<0.001$). Scores on all three tests decreased (non-significant) from MAXBROMO to POST1, scores recovered to near MAXBROMO levels by POST2. 3. Bromocriptine was not associated with improvements in mood state.

PEDro=Physiotherapy Evidence Database rating scale score (Moseley et al., 2002a).

Discussion

The effect of bromocriptine on cognitive function in patients with ABI was explored in one RCT (McDowell et al., 1998), and one case series (Powell et al. 1996). Low-dose bromocriptine (2.5 mg daily) improved functioning on tests of executive control including a dual task, Trail Making Test, the Stroop test, the Wisconsin Card Sorting Test and the controlled oral word association test (McDowell et al., 1998). However, bromocriptine did not significantly influence working memory tasks. Although McDowell et al. (1998) demonstrated some benefits following administration of bromocriptine, there was only a single administration of bromocriptine and the dose was considerably lower than that given by other studies that did not meet our criteria. Spontaneous recovery may have been a factor leading to the improved abilities in individuals receiving a single dose (2.5 mg daily) of the medication; however, study results did not answer this question. Powell et al. (1996) conducted a multiple baseline design on 11 patients with TBI or subarachnoid hemorrhage who received bromocriptine. Improvements were found on all measures assessed (memory, attention, motivation spontaneity) except mood, creating conflicting results between these two studies. The last RCT investigating the effects of bromocriptine was conducted 20 years ago; newer studies are required to fully determine the potential of bromocriptine as a treatment for general and executive cognitive functions.

Conclusions

There is conflicting level 2 (against) and level 4 (for) evidence as to whether or not bromocriptine may improve executive or general cognitive functioning following ABI.

Bromocriptine may improve other measures of cognition such as attention, but its effects on generalized cognition are conflicting. More research is required.

6.3.2.6 Growth Hormone (GH) Replacement Therapy

Following an ABI, it is not uncommon for individuals to be diagnosed with hypopituitarism. It is estimated that as many as 25 to 40% of individuals with a moderate to severe ABI demonstrate chronic hypopituitarism (Bondanelli et al., 2007; Kelly et al., 2006; Schneiderman et al., 2008). Despite this, few patients are screened for GH deficiencies; thus, the link between cognitive impairment and growth hormone deficiencies has not yet been definitively established (High et al., 2010). The benefits of GH replacement therapy on patient's executive and general cognitive function post TBI is investigated below.

Table 6.39 The Effect of rh (GH) on Executive and Cognitive Functioning Post ABI

Author Year Country Research Design PEDro Sample Size	Methods	Outcome
High Jr et al. (2010) USA PEDro=8 N=23	**Population:** TBI. *Placebo* (n=11): Mean Age=39.1 yr; Time Post Injury=5.1 yr. *Active rhGH* (n=12): Mean Age=36.1 yr; Time Post Injury=11 yr. **Intervention:** Participants were randomized to either a growth hormone replacement injection (rhGH) group or a placebo injection. Initially the drug was administered at 200 *ug*, followed by a 200 *ug* increase every month until the dosage reached 600 *ug*. Both groups received these injections for one year. **Outcome Measure:** Wechsler Adult Intelligence Scale-III, Delis-Kaplan Executive Function System.	1. Overall study results did not show great improvements on the majority of assessments between groups. 2. There was a significant improvement on the Finger tapping demonstrated in the treatment group. 3. Processing Speed Index: the treatment group improved significantly over the one-year period (p<0.050). The control group showed improvement at the end of the first 6 mo (p<0.010) but this was not seen at the end of the 1 yr. 4. Significant improvement was also noted on the Wisconsin Card Sorting Test (executive functioning) for the treatment group (p<0.010). 5. On the California Verbal learning Test-II improvement was noted for the treatment group on learning and memory.
Moreau et al. (2013) France PCT N=50	**Population**: TBI. Treatment Group (TG, n=23): Mean Age=37.9 yr; Gender: Male=19, Female=4; Mean Time Post Injury=7.8 yr; Mean GCS=8.1. Control Group (CG, n=27): Mean Age=37.1 yr; Gender: Male=24, Female=3; Mean Time Post Injury=5.5 yr; Mean GCS=9.4. **Intervention**: Participants were allocated to receive GH therapy (TG, 0.2-0.6mg/d) or no treatment (CG) for 1yr. Outcomes were assessed before (T1) and after (T2) treatment. **Outcome Measures**: Activities of Daily Living (ADL); Quality of Life Brain Injury (QOLBI); Verbal Memory (VM); Rey Complex Figure (RCF); Reaction Time (RT).	1. Both groups showed significant improvement in instrumental ADL (iADL, p=0.001) at T2, but not personal ADL (pADL). 2. Both groups showed significant improvement in QOLBI total scores (p=0.019) and intellectual (p=0.001), functional (p=0.023), and personal (p=0.044) subscores at T2, but not physical, psychological, and social subscores. 3. Both groups showed significant improvement (p<0.050) in aspects of attention (RT), memory (VM), and visuospatial (RCF) abilities at T2. 4. The TG showed significantly greater improvement in QOLBI functional (p=0.023) and personal (p=0.019) subscores, as well as RCF (p=0.037), but no significant difference was found for other outcome measures.

		5. There was a significant correlation (p<0.050) between QOLBI total and pADL (r=0.49). 6. There was a significant negative correlation (p<0.01) between attention (RT) and pADL (r=-0.59) and iADL (r=-0.56).
Reimunde et al. (2011) Spain Cohort N=19	**Population:** TBI; Gender: Male=19, Female=0. With Growth Hormone Deficiency (GHD) Group (n=11): Mean Age=53.36 yr; Mean Time Post Injury=44.55 mo. Without GHD group (n=8): Mean Age=47.12 yr; Mean Time Post Injury=46.6 mo. **Intervention:** Those with GHD received recombinant human GH (rhGH), subcutaneously (0.5 mg/d for 20d then 1 mg/d for 5 d). Those without GHD were given a placebo. Cognitive rehabilitation was given to everyone (1 hr/d, 5d for 3 mo). **Outcome Measure:** Weschler Adult Intelligence Scale (WAIS).	1. Results of the WAIS indicated that the control group improved significantly on the digits and manipulative intelligence quotient (p<0.050). 2. For those in the treatment groups improvement was noted in cognitive parameters: understanding digits, numbers and incomplete figures (p<0.050) and similarities vocabulary, verbal IQ, Manipulative IQ, and total IQ (p<0.010).

PEDro=Physiotherapy Evidence Database rating scale score (Moseley et al., 2002a).

Discussion

A 2010 RCT compared the long term (6 months and 1 year) effects of rhGH administration to placebo in a TBI population (High Jr et al. 2010). Significant improvements were noted in processing speed, executive functioning (Wisconsin Card Sorting Test), and learning (California Verbal learning test II) for both he rhGH and placebo groups. It is important to note while processing speed also improved in both groups at 6 mo, the improvement was only sustained in the treatment group at 1 year. Further positive results were reported in a more recent PCT by Moreau et al. (2013). Patient quality of life, instrumental activities of daily living, attention, memory and visuospatial ability improved over the treatment period in both the treatment and control group. However, the treatment group improved significantly more in the functional and personal subscales of quality of life assessments. Reimunde et al. (2011) also examined the use of recombinant human growth hormone in a cohort study. Results of the study indicate that those receiving the rhGH improved significantly on the various cognitive subtests such as: understanding, digits, numbers and incomplete figures (p<0.05), verbal IQ, Manipulative IQ, and Total IQ (p<0.01). The control group also showed significant improvement but only in digits and manipulative intelligence quotient (p<0.05). Of note IGF-I levels were similar between both groups at the end of the study.

Conclusions

There is level 1b evidence that recombinant human Growth Hormone (rhGH) is superior to placebo at improving processing speed (6 mo), executive function and learning in patients post TBI.

There is level 2 evidence that growth hormone (GH) therapy is effective for improving quality of life, instrumental activities of daily living (iADL), attention, memory, and visuospatial ability in patients post TBI.

There is level 2 evidence that recombinant human Growth Hormone (rhGH) administration improves intelligence and other cognitive subtests in TBI patients with growth hormone deficiency compared to

TBI patients without; however, insulin-like growth factor-1 (IGF-1) levels may be the same between groups.

The administration of human growth hormones appears to have positive (although sometimes limited effects) on general and executive functioning in those with an ABI.

6.3.2.7 Rivastigmine

Rivastigmine is an acetylcholinesterase inhibitor which prevents the enzyme acetylcholinesterase from breaking down acetylcholine. This increases the concentration of acetylcholine in synapses. Acetylcholine has been most strongly linked with the hippocampus and memory deficits; however, it is also implicated in attentional processing.

Table 6.40 The Effect of Rivastigmine on Executive and General Cognitive Functioning Post ABI

Author Year Country Research Design PEDro Sample Size	Methods	Outcome
Silver et al. (2006) USA RCT PEDro=9 N=123	**Population:** TBI. *Rivastigmine* (n=80): Mean Age=37 yr; Gender: Male=53, Female=27. *Placebo* (n=77): Mean Age=37.1 yr; Gender: Male=53, Female=24. **Intervention:** Participants were randomized to receive either rivastigmine (3-6 mg/d) or placebo. At the end of the first 4 wk, rivastigmine doses were increased to 3.0 mg, 2x/d. If necessary, doses were decreased to 1.5 mg or 4.5 mg 2x/d. **Outcome Measure:** Trails A and B, Hopkins verbal learning test (HVLT), Cambridge Neuropsychological Test Automated Batter Rapid Visual Information Processing (CANTAB RVIP A).	1. Results of the CANTAB RVIP A' and HVLT found no significant differences between the placebo group and the treatment group. 2. Rivastigmine was found to be well tolerated and safe.
Silver et al. (2009) USA RCT PEDro=9 N=127	**Population:** TBI. *Ex-Rivastigmine* (n=65): Mean Age=36.9 yr; Gender: Male=43, Female=22; Time Post Injury=73.5 mo. *Ex-placebo* (n=62): Mean Age=38 yr; Gender: Male=42, Female=20; Time Post Injury=100.1 mo. **Intervention:** Participants were randomized to receive rivastigmine injections (1.5 mg 2x/d to a max of 12 mg/d) or placebo injection. **Outcome Measure:** Trails A and B, Hopkins verbal learning test (HVLT), Cambridge Neuropsychological Test Automated Batter Rapid Visual Information Processing (CANTAB RVIP A).	1. The mean final dose of rivastigmine was 7.9 mg/day. 2. Forty percent of patients were responders on CANTAB RVIP A' or HVLT score at week 38. 3. At the end of the study period all (n=98) were seen to improve of the CANTAB RVIP A' ($p<0.001$), the HVLT ($P<0.001$), and the Trails A and B ($p<0.001$). 4. Sub-analysis controlling for order effects revealed there were no significant differences between groups.

Discussion

In two studies rivastigmine was administered to patients who had sustained a moderate to severe TBI (Silver et al., 2006; Silver et al., 2009). Neither RCT found significant effects of rivastigmine on measures of general or executive function. However, after controlling for order-effects, there were no significant effects of treatment.

Conclusions

There is level 1b evidence that rivastigmine is not effective for improving general or executive cognitive functioning, compared to placebo, following an ABI.

Rivastigmine is not effective in treating general or executive dysfunction post ABI.

6.3.2.8 Hyberbaric Oxygen Therapy

Hyperbaric oxygen therapy involves the inhalation of pure oxygen under pressure allowing the lungs to absorb more oxygen per breath. Currently hyperbaric oxygen therapy is used to treat decompression sickness, serious infections, and delayed wound healing as a result of a comorbid illness such as diabetes (The Mayo Clinic, 2019).

Table 6.41 The Effects of Hyperbaric Oxygen Therapy on General and Executive Functioning

Author Year Country Research Design PEDro Sample Size	**Methods**	**Outcome**
Hadanny et al. (2018) Israel Case Series N=154	**Population:** Mean age=42.7yr; Gender: Male=58.4%, Female=43.6%; Mean time post-injury=4.6yr; Injury severity: mild=44.8%, moderate=15.6%, severe=39.6%. **Intervention:** All individuals received hyperbaric oxygen therapy (HBOT). Sessions consisted of 60-90 mins of 100% oxygen at 1.5/2 ATA exposure 5 days a week. **Outcomes:** NeuroTrax software subsets: general, memory, executive functions, attention, information processing speed, visual spatial processing, motor skills.	1. On measures of general cognitive functioning there was a significant increase in scores after HBOT treatment ($p<0.0001$). 2. Memory scores significantly increased following HBOT treatment ($p<0.0001$). 3. Executive function scores significantly increased following HBOT treatment ($p<0.0001$). 4. Attentional scores significantly improved following HBOT treatment ($p<0.0001$). 5. Information processes speed significantly increased following HBOT treatment ($p<0.0001$). 6. Visual spatial processing significantly improved following HBOT treatment ($p=0.005$). 7. Motor skills significantly improved following HBOT treatment ($p<0.0001$).

Discussion

One recent case series has evaluated the potential benefits of hyperbaric oxygen therapy on general and executive functioning (Hadanny et al., 2018). This study used NeuroTrax to evaluate all neurocognitive measures. Both measures of general and executive functioning saw a significant improvement over the treatment period. However, it should be noted that this study did not contain a control group and therefore it is difficult to separate the effects of the treatment from spontaneous recovery.

Conclusions

There is level 4 evidence that hyperbaric oxygen therapy may improve general and executive functioning following an ABI.

Hyperbaric oxygen therapy may be beneficial for improving general and executive functioning following an ABI; however, more research is needed.

6.3.2.9 Dextroamphetamine

Dextroamphetamine is another central nervous stimulant, and similar to methylphenidate it is used to treat narcolepsy and attention deficit hyperactivity disorder. Dextroamphetamine is a non-catecholamine and sympathomimetic amine that acts as a stimulant, unfortunately more direct mechanisms of action are not currently known.

Table 6.42 The Effects of Dextroamphetamine on General and Executive Functioning

Author Year Country Research Design PEDro Sample Size	Methods	Outcome
Hart et al. (2018) United States RCT PEDro=10 N=32	**Population:** *DEX Group (N=17)*: Mean age=39.6yr; Gender: Male=11, Female=6; Mean GCS=8.2; Mean time post-injury=53.6dy. *Control Group (N=15):* Mean age=38.7yr; Gender: Male=15, Female=0; Mean GCS=7.5; Mean time post-injury=60.2dy. **Intervention:** Participants either received the placebo or 10 mg of dextroamphetamine (DEX). Each treatment was administered once a day, in the morning, for 3 weeks. **Outcomes:** Moss Attention Rating Scale (MARS), Hopkins Rehabilitation Engagement Rating Scale (HRER), Cognitive Failures Questionnaire (CFQ), Rating Scale of Attentional Behavior (RSAB), Finger Taping Test (FT), the Symbol Digit Modalities Test (SDMT), Disability Rating Scale (DRS), Agitated Behavior Scale (ABS), Profile of Mood States (POMS),	1. There was a significant difference between groups on the ABS (p=0.04), with the DEX group demonstrating more agitation over time. 2. No other significant differences were found.

Discussion

One RCT has recently evaluated the effects of dextroamphetamine on general and executive functioning using a variety of outcomes (Hart et al., 2018). Although dextroamphetamine was seen to significantly reduce agitation compared to the placebo group, no significant effects were seen on measures of cognition. Given the use of dextroamphetamine in other attentional disorders such as attention deficit hyperactivity disorder, the lack of results on any cognitive measures between these two studies is unexpected.

Conclusions

There is level 1b evidence that dextroamphetamine is not effective for the remediation of general cognitive functioning following an ABI.

Dextroamphetamine is moderate evidence to suggest that dextroamphetamine is not effective for the remediation of general functioning.

6.4 Verbal and Written Communication

Communication remediation focuses on one's ability to improve expressive language, speech production, reading, writing, and cognition. Due to impairments in cognitive abilities following an ABI, difficulties in producing proficient discourse is commonplace. Previous treatments have focused on improving narrative and structured conversations post injury (Kilov et al., 2009). Established treatments often focus on the individual's ability to communicate with a clinician or researcher but not in the presence of a friend or family member (Jorgensen & Togher, 2009). Whether an individual communicates with a friend, a family member or community member, rather than a trained clinician post brain injury, has had an effect on the language choices made by both partners (Jorgensen & Togher, 2009).

Group treatment may be an effective intervention for post ABI individualswith cognitive-communication deficits and may be used to target more complex and higher-level skills within the communication domain and with a wide array of communication partners. Within a group treatment setting, patients with ABI gain support and benefit from the experience of their peers within a non-judgmental environment to experiment with compensatory strategies and acquisition of appropriate interaction skills (College of Audiologists and Speech Language Pathologists of Ontario, 2002).

Some specific goals of group treatment post ABI include having individuals focus on having their basic needs met, improving word fluency, word usage and word finding, and, to have tools to help better organize ideas in conversation. Strategies to ensure meeting these goals is possible would be to implement the use of a yes/no response system, alphabet boards to serve as phonemic cueing for word retrieval, and word retrieval strategies. To improve clarity of speech and phonation, patients are encouraged to speak clearly and with vocal effort, all while receiving proper breath support. For clinical use, the Lee Silverman Voice treatment (LSVT®) would be the primary tool when addressing these issues.

6.4.1 Remediation of Verbal and Written Communication

Several authors have reviewed a variety of studies focusing on cognitive-communication therapies used to assist those post ABI (Coelho et al., 1996; Kennedy et al., 2008b; MacDonald & Wiseman-Hakes, 2010). In a review conducted by Coelho et al. (1996), the concluding findings suggest that those who sustain an ABI benefit from the work of an SLP. Study authors found evidence to suggest that individuals undergoing therapy showed gains in receptive and expressive language, speech production, reading, writing, and cognition. Further they noted that patients with more severe cognitive-communication deficits are more effectively remediated when treatment is directed toward the development of compensatory rehabilitation strategies such as the use of memory aids (Coelho et al., 1996). Additionally, Coelho and colleagues (1996) reported that although interventions directed at particular cognitive deficits are important, clinicians must attend to broader issues of social skills retraining, timing of treatment during recovery, treatment location and its effectiveness (e.g. hospital, home, school, work). Study results from Mackay et al. (1992) suggest that intervention programs offered earlier post injury result in shorter rehabilitation stays. Further, for individuals with comparable disabilities, those who receive rehabilitation have better than average cost outcomes compared to those not receiving these services (Aronow, 1987).

Table 6.43 Interventions for Improving Verbal and Written Communication

Author Year Country Research Design PEDro Sample Size	Methods	Outcomes
Barreca et al. (2003) Canada RCT PEDro=6 N=13	**Population:** ABI; Mean Age: 41.3 yr; Gender: Male= 10, Female= 3; Mean Time Post Injury=33 mo; Mean GCS=4.8. **Treatment:** Patients were assigned to an ABAB (n=7) or BABA (n=6) treatment sequence**.** Group A received an enriched stimulus environment, collaborative multi-disciplinary intervention, and additional yes/no response training (30 min, 3x/wk). Group B received standard intervention within a hospital environment. This took place over 8 wk, each interval being 2 wk. **Outcome Measure:** Western Aphasia Battery.	1. No order effect (AB vs BA; F=0.29; p=0.06) but a treatment trend was found for the effectiveness of group A over group B (A vs B; F=3.84; p=0.07). 2. No significant differences in Western Aphasia Battery scores between treatments at admission or 6 mo later (p>0.05).
Sumowski et al. (2014) USA Pre-Post N=10	**Population:** Severe TBI=10; Mean Age=42.8 yr; Gender: Male=6, Female=4; Mean Time Post Injury=8.4 yr. **Intervention:** Participants studied 48 verbal paired associates (VPAs) divided into 3 learning conditions: massed restudy (MR), spaced restudy (SR), and retrieval practice (RP). MR is similar to cramming, whereas SR is distributed learning. RP was similar to SR; however, re-exposure trials were framed as cued recall tests. Recall of VPAs was done at 30 min post intervention, and at 1 wk. Participants performed all 3 methods of learning. **Outcome Measure:** Recall of VPAs.	1. Participants recalled 46.3% of VPAs learned through RP compared with 12.5% through MR (p<0.0001), and 15% through SR (p=0.002). 2. SR did not result in better memory than MR (p=0.0555). 3. At 1wk, participants recalled 11.3% in the RP group compared to 0.0% in the MR (p=0.004), and 1.3% in SR (p=0.011). Again, SR and MR did not differ from each other (p=0.343).
Harvey et al. (2013) USA Pre-Post N=9	**Population:** Severe TBI=9; Mean Age=35.78 yr; Gender: Male=8, Female=1; Mean Time Post Injury=10.89 yr. **Intervention:** Participants read 24 passages in two different scenarios, once without any training and once after receiving 6 sessions of computerized text-to-speech training. **Outcome Measure:** Reading rate, comprehension accuracy.	1. Reading rates were significantly faster after receiving training (p=0.036). 2. No significant difference between text-to-speech and no text-to-speech conditions were noted for comprehension accuracy (p=0.950).
Brownell et al. (2013) USA Pre-Post N=8	**Population:** TBI=8; Mean Age=43 yr; Gender: Male=5, Female=3; Mean Time Post Injury=8.5 yr; Severity: Moderate to severe. **Intervention:** Therapy targeting difficulties interpreting figurative language. Participants were assessed at baseline and then performed metaphor interpretation probes and untrained line orientation tasks during the three study phases: (1) baseline phase (10 session, 2x/wk); (2) training phase with word tasks ranging in difficulty (2x/wk); and (3) post training phase	1. As a whole, the group significantly improved on the Oral Metaphor Interpretation following treatment compared to baseline (Mean difference score=5.9, p<0.001). 2. Scores on the Benton line Orientation task did not improve significantly (Mean difference score=-0.2, p=0.585) from pre to post training. 3. 6 of 8 participants improved significantly on metaphor interpretation following

Author Year Country Research Design PEDro Sample Size	Methods	Outcomes
	(10 sessions, 2x/wk). The exact number of sessions varied (total 23 to 34). Follow-up conducted at 3 to 4 mo post training. **Outcome Measure:** Oral Metaphor interpretation, Benton Line Orientation-Judgment Task Short Form Q.	training, 3 of which maintained these improvements at follow-up.
O'Neil-Pirozzi et al. (2010b) USA Prospective Control Trial N=94	**Population:** TBI; *Experimental Group*: Mean Age=47.3 yr; Mean Time Post-Injury=11.8 yr; *Control Group*: Mean Age=47.0 yr; Mean Time Post-Injury=13.4 yr **Treatment:** In a non-randomized pre-post study group comparison, participants in the experimental group were trained to use Internal Memory Strategies (I-MEMS; n=54); the intervention consisted of 12 90-min sessions, held 2x/wk for 6 wk. It included memory education and emphasized internal strategy acquisition to improve memory function from encoding, storage and retrieval perspectives; the control group (n=40) consisted of a convenience sample. **Outcome Measure:** Hopkins Verbal Learning Test-Revised (HVLT-R), Rivermead Behavioural Memory Test II (RBMT II). Patients were assessed on Week 1 (pretest), Week 7 (post-test 1), and Week 11 (post-test 2).	1. Pretesting revealed a significant difference between experimental and control groups on the HVLT-R only (p=0.02). 2. Individuals who had had a severe TBI performed more poorly on the HVLT-R than those with moderate injuries. 3. Although those with a severe injury did not improve as much as those with a mild or moderate injury, they did improve more than those in the control group at both post-test 1 (p=0.0002) and post-test 2 (p<0.0001). 4. Similar to what was found with HVLT-R assessments, severe injury predicted worse RMBT II scores than moderate injury. 5. RBMT II scores in the I-MEMS groups revealed significant improvements at both post-test 1 (p=0.045) and post-test 2 (p=0.0013) relative to control. 6. Overall memory performance was improved for all those in the experimental group compared to the control group.

Discussion

Barreca et al. (2003) compared two rehabilitation approaches that attempted to establish correct responses to yes/no questions. In addition to providing an enriched environment to the first group, a communicative disorders assistant provided yes/no training to the individuals. In addition, the assistant trained healthcare team members and families to follow scripted procedures to increase arousal/attention and to elicit yes/no responses. This was compared against standard care. Despite no significant differences on the Western Aphasia Battery, families reported on a satisfaction questionnaire that they were better able to communicate with their loved one (Barreca et al., 2003).

Another study examined retrieval practice, administered in person, compared to massed restudy and spaced restudy (Sumowski et al., 2014). In the retrieval practice intervention, the participants were first exposed to a verbal paired associate; the subsequent trials for that verbal paired associate were structured as cued recall tests. For individuals with severe TBI and memory-impairments, this retrieval practice was significantly more effective for memory recall than the massed restudy and spaced restudy interventions both immediately following the intervention and at 1 week post (Sumowski et al., 2014).

Technology interventions have also been used to improve communication post TBI. In a study conducted by Harvey et al. (2013) participants completed six sessions of computerized text-to-speech training. Results showed a significant improvement in reading rates during the text-to-speech conditions compared to the no text-to-speech conditions (Harvey et al., 2013). These findings suggest that text-to-speech technology is a useful tool in improving reading rates among individuals with a TBI. However, the authors note that while reading rates improved, comprehension of the written material was not affected.

Brownell et al. (2013) utilized therapy targeting deficiencies in figurative language. All participants completed 10 sessions of word task training resulting in significant improvements in oral metaphor interpretation (Brownell et al., 2013). Participants in the study were approximately eight years post injury suggesting that post TBI individuals are capable of advanced improvements in non-literal language even after the period of rapid and pronounced spontaneous recovery.

In a study by O'Neil-Pirozzi et al. (2010b), individuals with ABI participated in twelve 90-minute sessions which were held twice a week. The intervention included memory education, and to improve memory function the study emphasized internal strategy acquisition. Primary emphasis was placed on semantic association followed by semantic elaboration/chaining and imagery. Results from the Hopkins Verbal Learning Test (HVLT) indicated significant differences between the groups and those with a severe ABI performed more poorly than those with a moderate injury. Despite this finding, those with severe ABIs did perform better than those in the control group. In all, memory performance was seen to improve for all in the intervention group compared to the control group, however this relationship was slightly modified by injury severity.

Conclusions

There is level 1b evidence that yes/no training and an enriched environment does not significantly improve communication responses in individuals with an ABI.

There is level 4 evidence that retrieval practice is more effective for memory recall in individuals with an ABI than massed restudy (i.e., cramming) and spaced restudy (i.e., distributed learning).

There is level 4 evidence that targeted therapy towards figurative language improves communication in chronic TBI individuals.

There is level 4 evidence that text-to-speech technology improves reading rates post ABI but not reading comprehension.

There is level 4 evidence that cognitive-communication therapy targeting the interpretation of figurative language is effective for improving language and metaphor comprehension following an ABI.

Communicating "yes/no" responses with consistent training and environmental enrichments does not improve communication responses in individuals post ABI.

Retrieval practice is effective for improving verbal communication in individuals with an ABI.

Targeted figurative language therapy improves communication and comprehension in individuals with TBI; although the severity of the injury may moderate these effects.

Text-to-speech technology improves reading rates in individuals with TBI, but not comprehension.

6.5 Social Communication Skills Training for Individuals and Communication Partners

After an ABI, issues may present in either verbal or nonverbal communication skills; difficulties with conversation may include topic introduction, topic maintenance, topic choice, turn taking and perspective taking (College of Audiologists and Speech Language Pathologists of Ontario, 2002)

Pragmatics describe "a person's ability to perceive, interpret and respond to the contextual and situational demands of conversation" (Wiseman-Hakes et al., 1998). In other words, pragmatics refers to the interaction between language behavior and the context in which language occurs (Strauss HM & RS, 1994). Studies have shown that the conversations of individuals with ABI, compared to individuals without injury, have been rated as significantly less interesting, less appropriate, less rewarding, more effortful, and more reliant on conversation partners to maintain the flow of the conversation (Bond & Godfrey, 1997; Coelho et al., 1996). Since it is through conversation that we form and maintain relationships, impaired communication can have a significant negative impact on social competence, vocational competence and academic competence. Social communication deficits in ABI can result in social isolation, frustration, and a sense of helplessness (Kilov et al., 2009; Sarno et al., 1986).

6.5.1 Social Communication Skills Training

ABI can influence every aspect of life including physicality, cognitive function, emotional responses, and social functioning. Social communication training more specifically addresses social competence and removing barriers to returning to a meaningful and productive life, which includes having the ability to sustain interpersonal relationships (Braden et al., 2010). Communication remediation focuses on one's ability to improve expressive language, speech production, reading, writing, and cognition.

Table 6.44 The Effectiveness of Social Communication Skills Training Post ABI

Author Year Country Research Design PEDro Sample Size	Methods	Outcomes
Westerhof-Evers et al. (2017) Netherlands RCT PEDro=7 $N_{Initial}$=61 N_{Final}=56	**Population:** TBI; Mean Age=43.2 yr; Gender: Male=83, Female=17; Severity: Moderate to severe. **Treatment:** Participants were randomly assigned to receive Treatment for Impairments in Social Cognition and Emotion Regulation (T-ScEmo, n=30) protocol or Cogniplus (n=29) training. The TScEmo protocol is aimed at enhancing emotion perception, perspective taking, theory of mind, goal-directed social behaviour through 20 individual treatment sessions offered 1-2x/wk by neuropsychologists. Cogniplus is an individually administered computerized attention training aimed at improving general cognition. Outcomes were assessed baseline (T0), post-intervention (T1), and 3-5 mo follow-up (T2).	1. For the primary outcome of TASIT-short, there was no significant improvements over time in either group or no significant differences between groups. 2. Significant Time x Group interactions from T0 to T1 were observed for FEEST (p=0.01), CT (p=0.02), RRL (p<0.01), and TGA (p<0.01). No significant interactions from T0 to T1 were observed for FP, DEX-Soc-self, DEX-Soc-proxy, BAFQ-SM-self, BAFQ-SM-proxy, BAFQ-Emp-self, BAFQ-Emp-proxy, QOLIBRI satisfaction, QOLIBRI burden, RQS-self, RQS-life partner, WAIS-III digit span, TMT A, TMT B/A, or TEA lottery.

Author Year Country Research Design PEDro Sample Size	Methods	Outcomes
	Outcome Measure: The Awareness of Social Inferences Test (TASIT-short), Sixty faces test (FEEST), Cartoon test, Faux Pas test (FP), Wechsler Adult Intelligence Scale (WAIS-III digit span), Trail Making Test (TMT A and B/A), Test of Everyday Attention Lottery (TEA lottery), Dysexecutive Questionnaire-Social scales (DEX-Soc-self, DEX-Soc-proxy), Brock's Adaptive Functioning Questionnaire-Social monitoring scale (BAFQ-SM-self, BAFQ-SM-proxy), BAFQ empathy scale (BAFQ-Emp-self, BAFQ-Emp-proxy), Role Resumption List (RRL), Quality of Life after Brain Injury (QOLIBRI satisfaction, QOLIBRI burden), Treatment Goal Attainment (TGA), Relationship Quality Scale (RQS-self, RQS-life partner).	3. Significant Time x Group interactions from T0 to T2 were observed for FEEST (p<0.01), CT (p=0.02), BAFQ-Emp-proxy (p=0.02), RRL (p<0.01), QOLIBRI burden (p=0.04), RQS-life partner (p=0.02), and TGA (p<0.01). No significant interactions from T0 to T2 were observed for FP, DEX-Soc-self, DEX-Soc-proxy, BAFQ-SM-self, BAFQ-SM-proxy, BAFQ-Emp-self, QOLIBRI satisfaction, RQS-self, WAIS-III digit span, TMT A, TMT B/A, or TEA lottery.
Dahlberg et al. (2007) USA RCT PEDro=6 N=52	**Population:** TBI; Mean Age=41.17 yr; Gender: Male=44, Female=8; Mean Time Post Injury=9.67 yr; Severity: Severe=40, Moderate to mild=12. **Treatment:** Patients were randomly assigned to either the experimental (n=26) group or the control group (n=26). Individuals receiving the training focused on listening to others, communicating needs, and regulating their emotions during social interactions. There were 12 sessions each lasting 1.5 hr. The control group waited 3 mo before undergoing treatment. Patients were assessed 5 times: baseline (wk 0), end of treatment (wk 12), at wk 24, 36 and 48. **Outcome Measure:** Profile of Functional Impairment in Communication (PFIC), Social Communication Skills Questionnaire-Adapted (SCSQ-A), Goal Attainment Scale (GAS).	1. Results of the PFIC rating scale showed significantly greater improvements on 7 of the subscales included on the PFIC: general participation (p=0.001), quantity (p=0.024), internal relation (p=0.009), external relation (p=0.005), clarity of experience (p=0.024), social style (p<0.001) and aesthetics (p=0.014). 2. The SCSQ-A showed significant improvement (p=0.005) for the treatment group compared to the control, pre- and post-intervention. 3. Over time significant improvement were noted between baseline scores and post-treatment scores for all participants receiving training on the PFIC (21 of the 30 subscales: p<0.001). Significant improvement was noted on the SCSQ-A (p<0.001) as well. 4. Significant improvements were made on the GAS from baseline to all post-treatment evaluations (p<0.001).
Bosco et al. (2018) Italy Pre-post N=19	**Population:** *Severe TBI:* Mean age=38.5yr; Gender: Male=16, Female=3; Mean time post-injury=99.4 months; GCS<8. **Intervention:** Groups of 5-6 participants met twice a week for 12 weeks for a total of 24 Cognitive Pragmatic Treatment (CPT) sessions. Participants were assessed at four time points, 3-months pretreatment, immediately before treatment, immediately following treatment, and 3-months post-treatment. **Outcomes:** Assessment Battery for Communication (ABaCo), Communications Activities of Daily Living (CADL), Aachener Aphasie test, Attentional Matrices, Trail Making test, Verbal Span, Corsi's Block-Tapping test, immediate and deferred recall test, Tower of London test, Modified Card Sorting	1. There was a significant difference in scores on the ABaCO between pretreatment and posttreatment scores (p<0.001). There were no significant differences between the two initial time points or the two posttreatment timepoints. 2. Similar results were seen for the CADL, with individuals showing a significant improvement in their functional communication skills following treatment (p=0.024). 3. Between immediate pretreatment scores and immediate posttreatment scores significant differences were only seen on the Verbal Span (p=0.045), and the Modified Card Sorting test (p=0.004).

Author Year Country Research Design PEDro Sample Size	Methods	Outcomes
	test, Raven Colored Progressive Matrices, Sally & Ann, Strange Stories.	
Finch et al. (2017) Australia Pre-Post N=8	**Population:** TBI; Mean Age=36.25 yr; Gender: Male=4, Female=4; Mean Time Post Injury=24.6 mo; Mean GCS=8.25; Severity: moderate=1, severe=7. **Treatment:** Participants received one 1 hr group and one 1 hr individual therapy session per wk for 8 wk. Therapy sessions were led by a speech-language pathologist and focussed on remediating impaired social communication skills using metacognitive strategy instruction training and goal-based therapy. Outcomes were assessed at baseline (4 wk baseline prior to intervention, pre-intervention, post-intervention, and 4 wk follow-up. **Outcome Measure:** Profile of Pragmatic Impairment in Communication (PPIC), LaTrobe Communication Questionnaire (LCQ), Goal Attainment Scaling (GAS).	1. For PPIC, only the literal content (p=0.005), general participation (p=0.02), internal relation (p=0.008), clarity of expression (p=0.026), and aesthetics (p=0.016) subscales showed significant improvement from baseline to 4 wk follow-up. No significant differences were observed for the quantity, quality, external relation, social style, or subject style subscores. 2. For PPIC, only the aesthetics subscale was significantly improved (p=0.039) comparing post-intervention to pre-intervention. 3. No significant differences for LCQ were observed when comparing baseline to 4 wk follow-up or pre- to post-intervention. 4. During the intervention, participants identified between three and six goals each. Following the intervention, there was a significant increase in GAS goal T-scores (p=0.012).
Llorens et al. (2012) Spain Pre-Post N=10	**Population:** ABI=10; Mean Age=41.1yr; Gender: Male=7, Female=3; Mean Time Post Injury=402.2d. **Intervention:** Participants underwent sessions (1hr/wk for 8mo) using an interactive touch screen-based game asking questions related to knowledge, reasoning, action, and cohesion in groups of ≤4. Testing of participants occurred at baseline and post intervention. **Outcome Measure:** Self-Awareness Deficits Interview (SADI), Social Skills Scale (SSS).	1. On the SADI, after treatment all participants perceived their deficits properly compared to only 4 participants at baseline; 2 participants had difficulty perceiving their disability post treatment compared to 7 participants at baseline and 5 participants had difficulty establishing realistic goals post treatment compared to 7 at baseline. 2. On the SSS at baseline, 6 participants showed altered levels in social skills, compared to 2 following treatment.
Braden et al. (2010) UK Cohort $N_{initial}$=30 N_{final}=17	**Population:** TBI; Mean Age=42.11 yr; Gender: Male=21, Female=9; Mean Time Post Injury=7.85 yr. **Treatment:** Participants received Group Interactive Structured Treatment (GIST) for social competence. This program was provided in a rehabilitation facility or in the community. A treatment workbook, developed specifically for GIST, was given to each participant. Each group member was asked to attend 13, 1.5 hr/wk sessions to discuss various topics related to effective communication. Patients were assessed at baseline, post-treatment, and at 3 and 6 mo. **Outcome Measure:** Profile of Pragmatic Impairment in Communication (PPIC), Social Communication Skills Questionnaire-Adapted (SCSQ-A), Goal Attainment Scale (GAS), Satisfaction	1. Social communication skills, as assessed by SCSQ-A, GAS and SWLS, improved significantly pre- to post-assessment (p<0.05). 2. For those in the TBI+ group (those with a substance disorder, a psychiatric disorder, or other neurological complications) significant improvement was noted on their SCSQ-A, GAS, SWLS scores (p<0.01, p<0.000 and p=0.01 respectively). The improvement on the PPIC was not significant (p=0.40). 3. There were no significant differences comparing the groups (TBI only to TBI+) at baseline, post-intervention or 6 mo post-intervention for the PPIC, person ratings on SCSQ-A, GAS and SWLS.

Author Year Country Research Design PEDro Sample Size	Methods	Outcomes
	with Life Scale (SWLS).	

Discussion

An RCT by Westerhof-Evers et al. (2017) compared the use of a Social cognition and Emotion regulation treatment (T-ScEmo) to a treatment for general cognitive gains (Cogniplus) (control group), to evaluate how participants performed on emotion perception, social understanding, and social behavior. The T-ScEmo group had statistically significant improvements on emotion perception (facial affect recognition), theory of mind, proxy-rated empathic behavior, societal participation, and treatment goal attainment, when compared with the Cogniplus group (Westerhof-Evers et al., 2017). Participants in the T-ScEmo group also reported higher quality of life and their life partners rated relationship quality to be higher than those in the Cogniplus group.

In an RCT conducted by Dahlberg et al. (2007) it was found that subjects in the experimental group, when exposed to twelve, 1.5 hour communication sessions, significantly improved their scores on the general participation in conversation subscale on the Profile of Functional Impairment in Communication and the Social Communication Skills questionnaire-adapted (Dahlberg et al., 2007). These improvements were also noted at 6- and 9-month follow-up periods. It's worth noting that both Dahlberg et al. (2007) and Westerhof-Evers et al. (2017) interventions included components of emotional regulation.

Finch et al. (2017) conducted pre-post study in adults with brain injury aimed at improving and maintaining social communication skills, in particular, the study authors focused on improved perceived communication skills, and achievement of goals. The results from this study indicated that goal-driven and metacognitive strategy-based interventions may help individuals with TBI achieve social communication goals.

Braden et al. (2010) examined the efficacy of the Group Interactive Structured Treatment (GIST) for social competence in a cohort study examining 30 individuals greater than one year post ABI. The 13 week training reviewed the following topics: skills of the great communicator, self-assessment and goal setting, starting conversations, keeping conversations going and using feedback, assertiveness in solving problems, practice in the community, social confidence through positive self-talk, social boundaries, videotaping, video review, conflict resolution, closure and celebration (Braden et al., 2010). Overall, data gathered demonstrated significant positive effects of GIST on social communication. Further, the program seemed to be effective for individuals with TBI who also comorbidities had, as stratification revealed there were no significant differences between these groups in terms of outcome. Another study also examined the effects of group cognitive pragmatic therapy (Bosco et al., 2018). Individuals were seen to improve on measures of communication, communication in daily activities, and verbal span. Although this study demonstrated significant improvements in social and functional communication, there was no control group to determine the effects of this therapy compared to no or alternative therapies.

A final study used interactive touch screens to apply a game-based question activity, which included topics around knowledge, reasoning, action, and cohesion of thoughts (Llorens et al., 2012). Although formal statistical analysis was not performed, 6/10 participants initially showed altered levels of communication on the Social Skills Scale, compared to only 2/10 post-treatment.

Conclusions

There is level 1b evidence that the Social Cognition and Emotion Regulation protocol when administered by a neuropsychologist is more effective for the remediation of social communication skills than the Cogniplus protocol in individuals with an ABI.

There is level 1b evidence that a variety of communication skills training programs improve social communication skills in individuals with an ABI, as well as self-concept and self-confidence in social communications.

There is level 4 evidence suggesting that a goal-driven, metacognitive approach to intervention may be beneficial in assisting individuals with TBI to achieve social communication goals.

There is level 4 evidence that interactive touch screen games focused on areas of reasoning, knowledge and action may be effective for improving social skills following an ABI.

There is level 2 evidence that the Group Interactive Structured Treatment program (GIST) is effective for improving social communication skills in those with a TBI as well as other neuropsychological comorbidities.

Training in social skills, social communication or pragmatics is effective in improving communication following brain injury.

Goal-driven interventions may be effective in improving social communication skills and goals following TBI.

Group Interactive Structured Treatment (GIST) is effective for improving social communication skills following an ABI.

Computer-based game programs which deliver cognitive-communication skills training may be effective for improving social skills.

6.5.2 Training Communication Partners

The success of communication interventions often relies on the understanding, compliance and competence of communication partners. Training of communication partners has become a central component of communication interventions with many populations. This development is consistent with the World Health Organization (2001) emphasis on *context* (environmental and attitudinal) as a determinant in health and disability outcomes. Training of communication partners has been shown to have a positive effect on communication effectiveness and reacquisition of communication skills in children with language disorders and developmental disabilities (Girolametto et al., 1994), adults with aphasia (Kagan et al., 2001), adults with dementia (Ripich et al., 1999), and adults with ABI (Togher et al., 2004).

Following an ABI individuals may have difficulty engaging in meaningful conversation with others. Training communication partners is particularly helpful in successfully facilitating communication with those with moderate to severe ABI. The strategies that are most useful in ensuring success of treatment include speaking in short, simple sentences, making and maintaining eye contact, and asking the patient to repeat the messages being conveyed (Behn et al., 2013). Also, asking patients to clarify that they understand the information and repeating the information when necessary, while allowing adequate time to receive an answer. Presenting the information in written form can also elicit a positive outcome from patients (Behn et al., 2013). Eliminating environmental distractions will be a tremendous aid to allow proper focus and attention for optimal results. Communication partners should present choices to patients and clarify the intent of the message being delivered. Using a variety of modes of communication (such as nonverbal) can also be a useful strategy (Behn et al., 2012, Togher et al., 2004, Togher et al., 2016, Sim et al., 2013, Togher et al. 2013).

Table 6.45 Strategies for Training Communication Partners for those with ABI

Author Year Country Research Design PEDro Sample Size	Methods	Outcomes
Behn et al. (2012) Australia RCT PEDro=6 N=15	**Population:** Caregivers=10, TBI=5. *TBI*: Mean Age=29.2 yr; Gender: Male=3, Female=2; Mean Time Post Injury=6.8 yr. **Treatment:** Caregivers were randomly assigned to a program on how to facilitate better conversations with individuals who had a TBI. The treatment group (n=5) participated in in a range of collaboration and elaboration conversational strategies (17 hr across 8 wk). Collaborative strategies were designed to encourage those with a TBI to participate more actively in conversations. The control group (n=5) was not trained. **Outcome Measure:** Adapted Measure of Support in conversation (MSC), Adapted Measure of Participation in Conversation, La Trobe Communication Questionnaire, Modified Burden Scale.	1. The trained group improved significantly on the MSC-acknowledging competence (p<0.001) and MSC-revealing competence (p=0.002). 2. Study results found paid caregivers were able to benefit from training; all participants were able to improve their communication skills with those who had sustained a TBI. 3. Trained caregivers also found they experienced greater levels of burden and described negative aspects of caring more often than those who were not in the paid group.
Togher et al. (2004) Australia RCT Crossover PEDro=5 N=40	**Population:** Police Officers=20, TBI=20**.** *TBI*: Gender: Male=20, Female=0; Mean Age=36.75 yr; Mean Time Post Injury=8.8 yr. **Treatment:** Patients were randomly assigned to interact with trained (treatment; n=10) or untrained (control; n=10) male police officers. Trained officers were provided with a 6 wk program targeting communication strategies using videos, theory, and transcripts **Outcome Measure:** Analyzed transcripts, Communication effectiveness.	1. Partner training resulted in more efficient and focused interactions, and fewer episodes of unrelated utterances by the people with ABI. 2. Trained communication partners were able to use strategies such as providing appropriate feedback and support during service encounter interactions, which enabled people with ABI to respond in an appropriate manner.

Author Year Country Research Design PEDro Sample Size	Methods	Outcomes
Togher et al. (2016) Australia PCT $N_{Initial}$=44 N_{Final}=38	**Population:** TBI; Gender: Male=26, Female=18. *Control (n=15)*: Mean Age=38.1 yr; Mean Time Post Injury=9.7 yr. *JOINT (n=14)*: Mean Age=30.3 yr; Mean Time Post Injury=8yr; *TBI SOLO (n=15)*: Mean Age=39.7 yr; Mean Time Post Injury=8.1 yr; **Treatment:** Participants were allocated to one of three groups: 1) control group, no training; 2) the JOINT group, attended all sessions together with their communication partner; or 3) the TBI SOLO group, attended sessions without their communication partner. The training was 2.5 hr/wk of group sessions and 1 hr/wk of individual sessions for 10 wk. Outcomes were assessed before and after treatment, and at 6 mo follow-up. **Outcome Measure:** La Trobe Communication Questionnaire (LCQ) - Self Report and Significant Other Report.	1. Post treatment, communication partners in JOINT reported greater overall improvements compared to TBI SOLO (p=0.05) and control (p<0.001). 2. Post treatment, individuals with TBI and their partners reported more positive change on LCQ in JOINT (p<0.001 for both) and TBI SOLO (p=.01; p=0.004) compared to controls, with only a significant difference on LCQ significant others reports between JOINT and TBI SOLO conditions (p=0.002). 3. At follow-up, individuals with TBI reported increase in positive change in communication skills in JOINT (p=0.01) and TBI SOLO (p=0.03) compared to controls, with no significant difference between JOINT and TBI SOLO. 4. At follow-up, more change was reported in communication partners in JOINT than TBI SOLO (p=0.01) and controls (p<0.001).
Sim et al. (2013) Australia PCT $N_{Initial}$=29 N_{Final}=27	**Population:** TBI; Gender: Male=24, Female=5. *JOINT Group (n=14)*: Mean Age=30.29 yr; Mean Time Post Injury=8.04 yr *Control Group (n=15)*: Mean Age=38.07 yr; Mean Time Post Injury=9.71 yr. **Intervention:** Participants and their everyday communication partners (ECPs) were allocated into either the JOINT training that received social communication training or a waitlist control group. The training was 2.5 hr/wk of group sessions and 1 hr/wk of individual sessions for 10 wk **Outcome Measure:** Exchange Structure Analysis (ESA), Productivity analysis, Information giving moves (K1), Information requesting or receiving moves (K2), Dynamic Moves (DM), Per Minute Speaking Time (PMST).	1. Those ECPs in the JOINT group, compared to controls, changed their use of questions more often (p=0.04) and their DM (information tracking/negotiation; p=0.07). 2. Participates with TBI in the JOINT group made greater improvements in PMST than controls (p=0.03). 3. No significant between group changes were identified for ECPS in K1 and K2. 4. No significant between group differences were determined for those with TBI in DM, K1, or K2.
Togher et al. (2013) Australia PCT $N_{Initial}$=44 N_{Final}=38	**Population:** TBI; Gender: Male=38, Female=6. *Control (n=15):* Mean Age=38.1 yr; Mean Time Post Injury=9.7 yr. *JOINT (n=14):* Mean Age=30.3 yr; Mean Time Post Injury=8 yr. *TBI SOLO (n=15):* Mean Age=39.7 yr; Mean Time Post Injury=8.1 yr. **Intervention:** Participants were allocated to one of three groups: 1) control group, no training; 2) the JOINT group, attended all sessions together with their communication partner; or 3) the TBI SOLO group, attended sessions without their communication partner. The training was 2.5 hr/wk of group sessions and 1 hr/wk of individual sessions for 10 wk. Training included role-play, listening to audio-recordings, practice	1. On the MPC, the JOINT group had greater improvements than the control group for both casual conversations (CC) and purposeful conversations (PC) on the Interaction scale (CC: p=0.01, PC: p=0.03) and on the Transaction scale (CC: p=0.003, PC: p=0.008). 2. The JOINT group made greater gains compared to the TBI SOLO group for Transaction scores in both conditions (CC: p=0.02, PC: p=0.01), and the Interaction scale for PC (p=0.03). 3. There were no significant differences between the TBI SOLO group and the control group on the MPC. 4. There were no significant between group differences on the MSC.

Author Year Country Research Design PEDro Sample Size	Methods	Outcomes
	interactions, and conversation strategies. Outcomes were assessed before and after treatment, and at 6 mo follow-up. **Outcome Measure:** Adapted Measure of Participation in Conversation (MPC), Adapted Measure of Support in Conversation (MSC).	5. At 6mo follow-up, there were no significant changes on outcome measures.

PEDro=Physiotherapy Evidence Database rating scale score (Moseley et al., 2002b).

Discussion

Studies examining communication partner training either focused on training individuals and their communication partners jointly (n=5), or independently (n=1). For the single study examining communication training interventions only for communication partners positive effects were still found (Togher et al., 2004). In a RCT conducted by Togher et al. (2004), the benefits of training individuals regarding how to effectively communicate with post ABI individualswas evident. Police officers were trained to respond to individuals with ABI, while the remaining officers who volunteered did not participate in the training. Overall, it was noted that trained officers significantly reduced the number of inquiries required to gain the necessary information from their callers, as well as spent less time establishing the nature of the service request and more time answering the questions being presented.

For studies using grouped training Behn et al. (2012) found that training allowed for caregivers to interact more easily with the individual with a TBI when strategies were used to encourage dialogue, this was compared to an untrained control group. The training in this study consisted of a number of didactic and performance-based approaches such as modeling, role-playing, feedback and rehearsal. As well, the strategies used were both elaborative and collaborative.

When examining training communication partners, the most efficacious way to improve interactions is to have both the individual with an ABI and their communication partner participate in training together. Two studies by Togher et al. (2013; 2016) found that those who completed social communication training together, made significantly greater gains in participation and overall communication compared to individuals with TBI who attended alone or those who received no training. In a similar study, providing training to communication partners allowed for their communication styles to be modified, which in turn allowed for the individual with TBI to improve their communication (Sim et al., 2013). This study highlighted the benefits of monitoring the two-way interaction using discourse analysis to ensure that information is given, received, and negotiated in an effective and appropriate way (Sim et al., 2013).

Conclusions

There is level 2 evidence to support the effectiveness of interventions that focus on training communication partners in the community, compared to no training, for improving interactions between responders and those with an ABI.

There is level 2 evidence that providing training to both the communication partner and the individual with a TBI together is more effective than only training the individual with TBI alone or no training at all.

Providing communication training to individuals who interact with people with TBI is effective and encourages two-way dialogue. **Providing training to the communication partner and the individual with TBI together is more effective than training the individual with TBI alone.**

6.5.3 Non-Verbal Communication

Goals of treatment regarding non-verbal communication post ABI include initiating conversation with others, learning to understand the emotion presented in verbal language, the ability to respond appropriately, and to maintain conversation. In order to achieve these goals, the necessary strategies to be employed consist of environmental and behavioural modification, counselling and support, pragmatic skills trailing, and targeted speech and language therapy. Patients will require positive reinforcement of the appropriate responses, as well as auditory/visual feedback by others.

Studies have shown that the conversations of individuals with ABI, compared to individuals without injury, have been rated as significantly less interesting, less appropriate, less rewarding, more effortful, and more reliant on conversation partners to maintain the flow of the conversation (Bond & Godfrey, 1997; Coelho et al., 1996). Since it is through conversation that we form and maintain relationships, impaired communication can have a significant negative impact on social competence, vocational competence and academic competence. Social communication deficits in ABI can result in social isolation, frustration, and a sense of helplessness (Kilov et al., 2009; Sarno et al., 1986).

6.5.3.1 Emotional Intelligence

Table 6.46 Effectiveness of Pragmatic and Emotional Intelligence Interventions

Author Year Country Research Design PEDro Sample Size	Methods	Outcomes
Westerhof-Evers et al. (2017) Netherlands RCT PEDro=7 $N_{Initial}$=61 N_{Final}=56	**Population:** TBI; Mean Age=43.2 yr; Gender: Male=83, Female=17; Severity: Moderate to severe. **Treatment:** Participants were randomly assigned to receive Treatment for Impairments in Social Cognition and Emotion Regulation (T-ScEmo, n=30) protocol or Cogniplus (n=29) training. The TScEmo protocol is aimed at enhancing emotion perception, perspective taking, theory of mind, goal-directed social behaviour through 20 individual treatment sessions offered 1-2x/wk by neuropsychologists. Cogniplus is an individually administered computerized	1. For the primary outcome of TASIT-short, there was no significant improvements over time in either group or no significant differences between groups. 2. Significant Time x Group interactions from T0 to T1 were observed for FEEST (p=0.01), CT (p=0.02), RRL (p<0.01), and TGA (p<0.01). No significant interactions from T0 to T1 were observed for FP, DEX-Soc-self, DEX-Soc-proxy, BAFQ-SM-self, BAFQ-SM-proxy, BAFQ-Emp-self, BAFQ-Emp-proxy, QOLIBRI satisfaction, QOLIBRI burden, RQS-self, RQS-life partner, WAIS-III digit span, TMT A, TMT B/A, or TEA lottery.

Author Year Country Research Design PEDro Sample Size	Methods	Outcomes
	attention training aimed at improving general cognition. Outcomes were assessed baseline (T0), post-intervention (T1), and 3-5 mo follow-up (T2). **Outcome Measure:** The Awareness of Social Inferences Test (TASIT-short), Sixty faces test (FEEST), Cartoon test, Faux Pas test (FP), Wechsler Adult Intelligence Scale (WAIS-III digit span), Trail Making Test (TMT A and B/A), Test of Everyday Attention Lottery (TEA lottery), Dysexecutive Questionnaire-Social scales (DEX-Soc-self, DEX-Soc-proxy), Brock's Adaptive Functioning Questionnaire-Social monitoring scale (BAFQ-SM-self, BAFQ-SM-proxy), BAFQ empathy scale (BAFQ-Emp-self, BAFQ-Emp-proxy), Role Resumption List (RRL), Quality of Life after Brain Injury (QOLIBRI satisfaction, QOLIBRI burden), Treatment Goal Attainment (TGA), Relationship Quality Scale (RQS-self, RQS-life partner).	3. Significant Time x Group interactions from T0 to T2 were observed for FEEST ($p<0.01$), CT ($p=0.02$), BAFQ-Emp-proxy ($p=0.02$), RRL ($p<0.01$), QOLIBRI burden ($p=0.04$), RQS-life partner ($p=0.02$), and TGA ($p<0.01$). No significant interactions from T0 to T2 were observed for FP, DEX-Soc-self, DEX-Soc-proxy, BAFQ-SM-self, BAFQ-SM-proxy, BAFQ-Emp-self, QOLIBRI satisfaction, RQS-self, WAIS-III digit span, TMT A, TMT B/A, or TEA lottery.
Neumann et al. (2015) USA RCT PEDro=9 $N_{Initial}$=71 N_{Final}=60	**Population:** TBI; *Faces (n=24)*: Mean Age=41 yr; Gender: Male=23, Female=1; Mean Time Post Injury=10.5yr; Mean GCS=6.9; *Stories (n=23)*: Mean Age=41.5 yr; Gender: Male=18, Female=5; Mean Time Post Injury=10.9 yr; Mean GCS=4.4; *Control (n=24)*: Mean Age=39.5 yr; Gender: Male=16, Female=8; Mean Time Post Injury=9.8yr; Mean GCS=5.3. **Treatment:** Participants randomly assigned to one of three interventions for 1 hr sessions 3 days/wk for 3 wk. Faces intervention taught individuals to recognize emotions in facial expressions, whereas stories intervention taught individuals to recognize emotion within stories. Control group underwent cognitive training. Participants assessed at pre-treatment and post-treatment within 4 days, at 3 mo and 6 mo. **Outcome Measure:** Diagnostic Assessment of Nonverbal Accuracy 2-Adult Faces (DANVA 2-AF), Emotional Inference from Stories Test (EIST), Interpersonal Reactivity Index (IRI), Neuropsychiatric Inventory (NPI) Irritability and Aggression domain.	1. According to DANVA 2-AF, participants trained in the face's intervention had a significant improvement across all follow-up time points compared to controls ($p=0.031$). 2. No significant improvement for the story's intervention on DANVA 2-AF compared to controls ($p=0.239$). 3. No significant improvement on EIST for the story's intervention ($p=0.167$) and faces ($p=0.349$) compared to controls. 4. Across all post-treatment assessments, there was a main effect of time as performance decreased for the story's intervention on EIST compared to controls ($p=0.001$). 5. NPI irritability and aggression and IRI empathy were not significant for faces or story interventions compared to controls.
McDonald et al. (2013) Australia RCT PEDro=6 N=20	**Population:** Severe TBI=16, CVA=3, Other=1; Mean Age=45.62 yr; Gender: Male=15, Female=5; Mean Time Post Injury=9.41 yr. **Treatment:** Patients were assigned to either a treatment group (n=10) or a control group (n=10). Patients receiving treatment attended 2hr/wk treatment sessions for 3	1. No significant treatment effects were found for the TASIT B, while accuracy on the prosody task ($p=0.074$) and rating of intensity of emotions ($p=0.076$) approached significance. 2. The treatment group showed a significant change on the self-report communication questionnaire ($p=0.013$).

Author Year Country Research Design PEDro Sample Size	Methods	Outcomes
	wk. Sessions consisted of a therapist and two participants. The program was tailored to focus on prosodic cues that may be seen in expressions of emotions. **Outcome Measure:** Awareness of Social Interference Test Form B-Part 1 (audio presentation), Prosodic Emotion Labelling Task, Communication Questionnaires.	
Radice-Neumann et al. (2009) USA RCT PEDro=5 N_{intial}=21 N_{final}=19	**Population:** TBI=19, ABI=2; Mean Age=43 yr; Gender: Male=12, Female=8; Mean Time Post Injury=12 yr; Mean GCS=4.08. **Treatment:** Patients were randomly assigned to receive either the facial affect recognition (FAR; n=10) training or the stories of emotional inference training (SEI; n=9). In the FAR training, individuals practiced identifying and discriminating emotions from facial expressions and focused on processing their internal emotions. SEI involved reading stories and answering questions. Sessions were 1:1 for 1 hr, 3 x/wk for 2-3 wk. **Outcome Measure:** Levels of Emotional Awareness Scale (LEAS), Diagnostic Assessment of Nonverbal Affect – adult faces/adult paralanguage (DANVA2-AF and DANVA2-AP), Brock Adaptive Functioning Questionnaire (BAFQ).	1. The FAR group improved on the DANVA2-AF over time (p<0.001), with changes being seen from pre-post (p<0.001) but not post to follow-up (p=0.244). 2. The SEI group also improved on the DANVA2-AF (p=0.006). The change occurred between the two pre-tests (p=0.004). 3. No significant changes were found for either group on the DANVA2-AP or the ability to infer emotions on video. 4. Both groups improved on their ability to infer emotions from contextual situations (LEAS; both p=0.019). 5. On the BAFQ, caregivers, indicated those in the FAR group showed improvement in the behaviour of patients (p=0.042); out of 4 emotional behaviours, only aggression changed significantly (p=0.047); SEI did not improve in perceived behaviour.
Gabbatore et al. (2015a) Italy Pre-Post $N_{Initial}$=20 N_{Final}=15	**Population:** TBI; Mean Age=36.7 yr; Gender: Male=10, Female=5; Mean Time Post Injury=76.13 mo; Mean GSC=4.5. **Treatment:** Participants received a control procedure with non-communication activities for 3 mo. This was followed by a 3-mo cognitive pragmatic training program (2 sessions/wk) consisting of 5-patient groups focussed on improving pragmatic abilities, self awareness, and executive function. **Outcome Measure:** Assessment Battery for Communication (ABaCo-comprehension, production, linguistic, extralinguistic, paralinguistic, and context), Attentive Matrices, Trail Making test, Verbal Span, Spatial Span, Immediate and Deferred Recall test, Tower of London test, Wisconsin Card Sorting test (WCST), Coloured Progressive Matrices Raven, Aachener Aphasie test-denomination scale (AAT), Sally and Ann Task, Strange Stories Task.	1. No significant improvements in ABaCo (production and comprehension) were observed during the nonspecific control period. 2. Participants showed significant improvements from pre-training to post-training for ABaCo comprehension (p<0.001), production (p<0.001), linguistic (p=0.005), extralinguistic (p=0.008), paralinguistic (p=0.02), and context (p=0.01). 3. At 3 mo follow-up post-treatment, AbaCo scores did not show significant differences from post-treatment. 4. From pre-training to post-training, no significant differences were observed for Verbal Span, Spatial Span, Attentive Matrices test, Trial Making test, Tower of London test, Raven's Colored Progressive Matrices, AAT, Sally and Ann task, or the Strange Stories task. Improvements were observed for the Immediate and Deferred Recall task (p=0.01) and Wisconsin Card Sorting test (p=0.003).

PEDro = Physiotherapy Evidence Database rating scale score (Moseley et al., 2002b).

Discussion

Westerhof-Evers et al. (2017) conducted an RCT describing social communication training. Not only did this study evaluate social understanding and social behaviour, it also examined emotional regulation and perception. On the emotional intelligence components of the study, the experimental group improved significantly on the facial affect recognition (Westerhof-Evers et al. 2017). Participants in the experimental group also reported higher quality of life and their life partners rated relationship quality to be higher than those in the control group (Westerhof-Evers et al. 2017).

A short treatment aimed at improving the ability to recognize emotional prosody was overall found to be ineffective (McDonald et al., 2013). Activities consisted of mostly games designed to focus on prosodic cues but found no change related to communication competence. Significance was approached for the treatment group in terms of improvements in the accuracy on the prosody task and ratings of intensity of emotions. However, participants in the treatment group self-reported that their ability to comprehend daily conversations had improved (McDonald et al., 2013).

Radice-Neumann et al. (2009) and Neumann et al. (2015) demonstrated that training focused on emotional processing (either by face affect recognition or by emotional inference training) can be effective when introduced to a group of individuals who had sustained an ABI. They assert that individuals with ABI can re-learn affective recognition skills. Two interventions to enhance emotion processing were utilized in both studies. The first intervention (Facial Affect Recognition), focused on attention to important visual information and attention to the participant's own emotional experience. The second intervention (Stories of Emotional Inference) taught patients to read emotions from contextual cues presented in stories and then relate these stories to personal events. Participants who received Facial Affect Recognition training had more positive outcomes (Neumann et al., 2015). Participants were better at reading faces (emotions) and were more descriptive in relating how they or others would feel in a similar situation. Decreased level of aggression was an additional finding.

The Stories of Emotional Inference group produced fewer improvements; however, they were able to make more emotional inferences about how they would feel in a given context. Individuals were still unable to make improvements in their ability to infer how others would feel in a given situation. The authors hypothesized that this might be related to self-centeredness, a trait often attributed to post ABI individuals(Radice-Neumann et al., 2009). However, Neumann et al. (2015) noted that the ability to identify one's own emotions is an important precursor to recognizing the emotions of others and therefore, should not be dismissed prematurely. The previous Radice-Neumann et al. (2009) RCT found slightly depressed effects compared to its 2015 follow-up. In 2009, groups were not significantly different from each other on the Diagnostic Assessment of Nonverbal Affect. However, both groups still significantly improved in their ability to infer emotions from contextual situations on the Levels of Emotional Awareness Scale (Radice-Neumann et al., 2009).

Gabbatore et al. (2015) evaluated a cognitive pragmatic rehabilitation program aimed at improving communicative-pragmatic abilities, in particular self-awareness and executive functioning. Study authors aimed at improving comprehension and production of a communication act. No improvements in comprehension were found from baseline to pre-training ($p=0.41$); however, significant improvements were demonstrated at post-training and follow-up (Gabbatore et al., 2015).

Conclusions

There is level 1b evidence that facial affect recognition training and emotional inference training is beneficial at improving the emotional perception of individuals with ABI.

There is level 1a evidence that the Treatment for Impairments in Social Cognition and Emotion Regulation and Cogniplus protocols are effective for improving emotional processing and emotional intelligence in individuals with an ABI.

There is level 1b evidence that short intervention designed to improve the ability to recognize emotional prosody was minimally effective in individuals with ABI.

There is level 4 evidence that a Cognitive Pragmatic Treatment (CPT) program is effective in improving communicative-pragmatic abilities in individuals with ABI.

Facial affect recognition and emotional interference training improves emotional perception post ABI.

Short intervention designed to improve emotional prosody is not effective post ABI.

Cognitive Pragmatic Treatment (CPT) program is effective at improving comprehension and production of a communication act.

The Treatment for Impairments in Social Cognition and Emotion Regulation and Cogniplus protocols are effective for improving emotional processing and emotional intelligence in individuals with an ABI.

6.5.4 Alternative and Augmentative Communication

Following severe ABI, patients present with significant communication challenges that interfere with daily communication needs. Whereas those who sustain a mild or moderate ABI may be more readily able to communicate using natural speech with minor difficulties, those with severe ABI may not be able to meet communication needs through speech alone and may benefit from an augmentative or alternative communication (AAC) strategy (Bourgeois et al., 2001b; Burke et al., 2004; de Joode et al., 2012; Fager et al., 2006; Johannsen-Horbach et al., 1985). Many individuals eventually recover their speech abilities post ABI, but there are still many who remain unable to speak for extended periods of time (Fager et al., 2006). For this specific group, assessments and AAC interventions may be a continual process, ensuring that the individual's level of function is matched appropriately with new systems as needed (Fager et al., 2006).

In the AAC domain, there are divisions of complexity that include simple, low-tech options (e.g. alphabet boards, picture-based communication boards, memory books, conversation books, day planners) and high tech options that include Voice Output Communication Aids (i.e., Dynavox, McCaw, Message Mate, Big Mack, Voice Pal and Boardmaker) (Fager et al., 2006). Notably, both low-tech and high-tech solutions to communication difficulties may have access that is either direct (i.e. touching/ pointing) or indirect (i.e. switch access or partner-assisted scanning).

Clinicians working in the area of AAC or Assistive/Enabling Technology are well acquainted with the recent explosion of technology options available. Presently, clinicians and patients have access to an extensive set of devices and peripherals including but not limited to iPad, Android, and Windows based tablets as well as a wide variety of associated applications and software (e.g. Proloquo2go, Talking Tiles). Changes in cost, improved ease of access/availability in mainstream retail, and rapid changes in the technology itself and associated applications have resulted in AAC clinical practice that is both invigorating and exhausting. Given that we are in the midst of unprecedented technology growth, the research in this area is lagging and limited.

In this particular area, difficulties sustained post ABI include verbal expression and severe dysarthria, with the primary goal of treatment being to allow individuals with severe ABI to efficiently access and communicate effectively via AAC. Particular treatment strategies for ACC may be to complete an initial assessment of the individuals needs from access and communication perspectives. From there, clinicians are able to determine the best device and method of access for individuals on a one-to-one basis (taking into account age and gender), and to allow time for training and teaching of both patient and communication partners (i.e. facilitator).

While there is a great deal of discussion around the importance of AAC, there is limited literature supporting the effectiveness of the strategies currently available for ABI populations. Further research is required in order to understand how these communication approaches or alternatives work to benefit individuals with an ABI and their care giving team.

6.5.4.1 Organizational Word Retrieval Strategies*:*

Burke et al. (2004) studied the use of three organizational word retrieval strategies for adults with ABI who use AAC. These organizational strategies included semantic topic, geographic place, and first letter of alphabet. While the subjects retrieved words more accurately when using the alphabet organization strategy, they expressed the preference for use of the semantic topic strategy. Clinicians may consider providing these three strategies for clients using AAC and assisting with identification of the most beneficial and preferred strategy for the individual client.

6.5.4.2 Non-Electronic Communication Board:

Assistive devices for AAC range in their properties and capabilities. Non-electronic communication boards, along with electronic counterparts, can aid post ABI individualswith messages and symbols depicted on the display. However, the number of messages they can display are limited, and they do not have the capacity for speech output (Iacono et al., 2011). This option would be ideal for people with complex communication needs, as they are easy to access, less expensive, and generally easier to use by patients, caregivers and clinicians.

6.5.4.3 Eye-Gaze Communication Board:

Assistive technologies aim to improve outcomes in individuals with physical and cognitive impairments. Gaze-based communication boards use computers controlled by the individual’s eyes. This device replaces keyboard and mouse with eye gaze for those who have physical impairments that prevents the use of upper limb motor function (Borgestig et al., 2016). By using their eyes, individuals can control the computer and gain access to communication and activities, including playing games, music, and perform a range of activities that they would not otherwise be physically able to do (Borgestig et al., 2016). The limitation of this technology is that is not as cost effective as other AAC devices, and novice users may experience fatigue quickly, as there is a substantial learning curve with the type of specific eye movements needed to operate the communication board (it does not mimic natural/intuitive eye movements required for daily activities) (Borgestig et al., 2016).

6.5.4.4 Bliss Symbols*:*

Bliss symbols or boards have been available and utilized for several years. The use of these symbols has been found to be very effective with those who have been diagnosed with aphasia or Broca's aphasia (Rajaram et al., 2012). However, there is little in the literature specifically pertaining to individuals with an ABI.

6.5.4.5 Pictograms:

Pictorgrams allow individuals to express their thoughts, emotions, wants and needs with pictures, as there is not a verbal explanation of all words. Pictogram-based ACC has been used for over 30 years and has been shown to help learn new linguistic skills(Pahisa-Solé & Herrera-Joancomartí, 2017).

6.5.4.6 Picture/Symbol Based Boards*:*

Despite the surge in technology, picture and symbol-based boards remain in high use today (e.g. pictograms, Boardmaker). These symbols or pictures may represent a concept, object, activity, place or event. Symbols, pictures, and boards in general may be used with minimal training and software may be individualized (Bhatnagar SC & F, 1999). The selection of symbols should be appropriate to the individual's communicative needs. Picture/symbol software is also available for computers, iPads, and iPhones.

Figure 1: Picture/Symbols

6.5.4.7 Alphabet Boards:

Individuals with dysarthria or who are non-verbal may benefit from an alphabet board. These boards are helpful for spelling single word or short phrase messages. Board sizes may vary depending on the person's abilities, necessity, or access (Bhatnagar SC & F, 1999). A lexical communication board is another type of AAC that uses common words such as nouns, pronouns, verbs and adjectives to improve sentence formation in patients, however this is not supported by academic sources and therefore requires further research.

6.5.4.8 Memory Aids:

The use of memory aids as an AAC tool has been studied extensively in patients with dementia and Alzheimer's, however their use in individuals with an ABI are not well documented. There are a number of different aids that can be used to compensate for memory loss and decline of cognitive and linguistic skills. Memory books are amongst the most popular and capitalize on procedural memory skills (page turning and reading aloud), they also promote transfer of information and increase social closeness (Bourgeois et al., 2001a). Memory aids help compensate for memory loss by helping to access stored information and memories, therefore they can be an extremely effective tool that are easily accessible and straightforward to use from a patient's perspective (Bourgeois et al., 2001a)

6.5.4.9 Synthetic Voice:

Synthetic voice, or synthesized speech uses computer-generated text-to-speech synthesis to extract speech and sound components from words and then combine them to form a natural sounding voice (JL Flaubert, 2017)This differs from digitized speech, which uses human voices stored as segments of sounds waves. Synthesized speech is ideal because it allows greater message flexibility and accuracy of what the individual is trying to convey (JL Flaubert, 2017).

6.5.4.10 Sign Language:

All the above AAC treatments are considered to be "aided" forms of communication, meaning they require external support by way of auxiliary materials (communication board, printed words, etc.) (Sigafoos & Drasgow, 2001). In contrast, natural gestures and sign language are forms of "unaided" AAC (Sigafoos & Drasgow, 2001)American Sign Language is the most commonly used, however there are other systems including Pidgin Signed English (PSE), and Signed Exact English (SEE). The advantages of sign language as an AAC are that it is portable (it does not require materials or devices), and it can be easier to teach than speech; communication partners, and clinicians can help individuals with hand formations (Sigafoos & Drasgow, 2001). There is no literature to support use of sign language in brain injured populations specifically, therefore more research in this field is required to make conclusions about its efficacy as a potential therapy.

Augmentative and alternative communication interventions designed to assist with organization, access, and efficiency of communication may be beneficial for individuals with severe ABI.

6.6 Conclusions

Cognitive interventions target a large variety of cognitive and cognitive-communication functions and deficits. The rehabilitation of these functions is complicated by the lack of consensus on the definition of attention, cognition, and general and executive functioning.

Comparing the efficacy of various remediation efforts is also complicated by cross-study variability in treatment duration (e.g. from 30 minutes once a day for 5 days to 5 hours, every day for 6 weeks).

Severity of injury and time since injury may also fluctuate from study to study. Over the past several years, Cicerone et al. (2000; 2005; 2011) reviewed a series of studies investigating the effectiveness of attentional retraining interventions during rehabilitation following traumatic brain injury and stroke. Not all patients respond equally to all intervention strategies and only a limited number of studies in the current review indicated whether severity of injury was related to the efficacy of a given intervention.

Communication impairments among this group are generally described as non-aphasic in nature (Ylvisaker M & SF, 1994). This is a different type of communication impairment than that seen following stroke, and this distinction is an important one. Communication deficits in individuals with ABI may also include aphasic-like symptoms such as naming errors and word-finding problems, impaired self-monitoring, and auditory recognition impairments. These constraints may also be coupled with other cognitive-communication impairments, such as attention and perception difficulties, impaired memory, impulsivity, and severe impairment of the individual's overall communicative proficiency within functional situations. These constraints can prevent individuals with ABI from exhibiting even simple communication skills (Lennox & Brune, 1993). (Amos, 2002)

Technology has increased the availability of external aids, although some seem more feasible to use than others (e.g., cell phones or hand-held recorders). Unfortunately, the studies reviewed did not specify the length of time subjects required to master compensatory strategies or the nature of the long-term effects. Generally, if these electronic appliances are used before the injury, they are more likely to be used post-injury as well. It was unclear from the studies if any of the participants had previous knowledge of these tools.

Most studies examined only tasks of word list recall and paired-associate learning suggesting that the mnemonic strategies reviewed may not generalize to other types of information (particularly real-world or functional information outside the laboratory). Errorless learning appears to be one procedure that can be used to enhance learning conditions. One study highlighted the difference between severity of impairment and ability to benefit from internal strategies.

Frequency of intervention has an impact on learning and retention, although the exact parameters of this are unclear at the present time. The optimal duration of a program is also open for speculation. No studies reviewed examined the number of sessions required for memory groups to be effective and only one study evaluated a difference in effectiveness between mild and severely impaired individuals after sessions.

6.7 Summary

There is level 2 evidence that drill, and practice training may not be effective for the remediation of attention compared to spontaneous recovery, regardless of the level of structure in the program for those with an ABI.

There is level 2 evidence that dual task training may be effective in improving attention task performance in ABI populations compared to non-specific training.

There is level 2 evidence that neither general nor name brand computer-based rehabilitation intervention may improve attention outcomes compared to usual care in ABI populations.

There is level 4 evidence that attention performance can be improved in ABI populations through repetition of tasks, either through computer-based or virtual reality environments.

There is level 2 evidence that adaptive training is no more effective than non-adaptive training in remediating attention in ABI populations.

There is level 1b evidence that emotional regulation therapy is not effective in treating attentional disorders compared to waitlist controls in ABI populations.

There is level 1b evidence that the addition of a therapy animal to attention training programs may enhance gains in concentration in those with an ABI.

There is level 2 evidence that mindfulness training compared to no intervention may improve an individual's ability to correctly reject inappropriate stimuli post ABI.

There is level 2 evidence to suggest goal management training, when compared to education, may be effective at improving attention in individuals post ABI.

There is level 2 evidence that goal management training is more effective in remediating task completion times than motor skill training, however it is not more effective in treating attention deficits, in individuals post ABI.

There is conflicting (level 2) evidence that attentional control or processing training may not significantly improve attention in post ABI individuals compared to control training.

There is level 4 evidence that summation tasks may be effective at improving attention in individuals post ABI.

There is level 4 evidence that a working memory training program may remediate attention in individuals post ABI.

There is level 4 evidence that cognitive rehabilitation therapy may not be effective for improving attention post ABI.

There is level 2 evidence that transcranial direct current stimulation when combined with an attention training program (compared to sham stimulation) may improve divided attention in individuals post ABI.

There is level 1b evidence that repeated transcranial magnetic stimulation compared to sham stimulation may improve attention following an ABI.

There is conflicting level 1b (positive) and level 2 (negative) evidence that donepezil may improve attention compared to placebo post ABI.

There is conflicting level 1a evidence regarding the effectiveness of methylphenidate following brain injury for the improvement of attention and concentration in individuals post ABI.

There is level 1a evidence that methylphenidate improves reaction time of working memory compared to placebo in individuals post ABI.

There is level 1b evidence that individuals carrying the Met allele may be more responsive to methylphenidate than those without the Met allele when it comes to the ABI population.

There is conflicting evidence as to whether bromocriptine improves performance on attention tasks compared to placebo in patients post TBI.

There is level 4 evidence that cerebrolysin may improve attention scores post ABI.

There is level 1b evidence that Rivastigmine compared to placebo is not effective for improving concentration or processing speed in post ABI individuals but may increase vigilance.

There is level 1b evidence that amantadine is not effective for improving attention compared to placebo following an ABI.

There is level 4 evidence that hyperbaric oxygen therapy may improve both attention and processing speed following an ABI.

There is level 1b evidence that dextroamphetamine does not improve attention following an ABI.

There is level 4 evidence that the NeuroPage system may increase a patient's ability and efficiency to complete tasks post TBI.

There is level 2 evidence that voice organizer programs are effective at improving recall of goals and are found to be effective by post TBI patients.

There is level 1b evidence that the use of a personal digital assistant (PDA) in combination with conventional occupational therapy is superior to occupational therapy alone at improving memory in patients post TBI.

There is level 2 evidence that personal digital assistants (PDAs) are superior to a paper-based schedule book at improving task completion rates post TBI.

There is level 1b evidence that use of a personal digital assistant (PDA) after receiving systematic instructions is superior to PDA trial and error learning at improving the number and speed of correct tasks post TBI.

There is level 1b evidence that reminder text messages sent to patients through their smartphones, whether alone or in combination with goal management training, improves goal completion post TBI.

There is level 2 evidence that a television assisted prompting (TAP) system is superior to traditional methods of memory prompting (paper planners, cell phones, computers) at improving the amount of completed tasks post TBI.

There is level 1b evidence that the audio-verbal interactive micro-prompting system, Guide, can reduce the amount of support-staff prompts needed for the patient to complete a task post TBI.

There is level 4 evidence that a computerized tracking system that sends reminders to patients when they are moving in the wrong direction reduces the amount of support-staff prompts needed for patients to complete a task post TBI.

There is level 2 evidence the use of an electronic calendar is superior to the use of a diary for improving memory in individuals with an ABI.

There is level 2 evidence that the presence of a diary with or without self-instructional training improves memory following an ABI.

There is level 2 evidence that the presence of a calendar may not improve orientation post ABI.

There is level 2 evidence that diary training in combination with self-instructional training may be more effective than diary training alone at improving memory and task completion post ABI.

There is level 4 evidence that virtual reality (VR) training may improve learning performance post ABI, even in the presence of distractions.

There is level 2 evidence that virtual reality training combined with exercise may be promising for improving memory outcomes and has a positive impact on visual and verbal learning when compared to no treatment.

There is level 2 evidence that virtual reality training may be superior to reading skills training at improving immediate and general components of memory for those with an ABI.

There is level 2 evidence that the format of route learning (either real or virtual reality based) does not significantly impact any improvements in memory as a result of route learning strategies for those with an ABI.

There is level 1b evidence to support self-imagination as an effective strategy to improve memory compared to standard rehearsal for those with an ABI.

There is Level 2 evidence to support that spaced retrieval training is an effective memory strategy when compared to massed retrieval or rehearsal in ABI populations.

There is level 2 evidence that strategies that utilize methods of multiple encoding, compared to strategies which only use singular methods, are more superior for improving memory post ABI.

There is level 4 evidence that errorless learning is more effective than errorful learning when it comes to improving memory in ABI populations.

There is level 1b evidence that hypnosis compared to no treatment may not be effective at improving memory in individuals post ABI.

There is level 1b evidence that individual memory therapy is no more effective than group memory therapy for those with an ABI.

There is level 2 evidence that programs involving multiple learning strategies (such as modelling, reciting, verbal instruction, and observation) are more effective than singular strategies for those with an ABI.

There is level 1b evidence that the Short Memory Technique may not be more effective than standard memory therapy at improving memory in individuals post ABI.

There is level 1b evidence that the Categorization Program, and Strategic Memory and Reasoning Training (SMART) may be effective for improving memory compared to standard therapy in individuals with an ABI.

There is level 2 evidence that time pressure management training is no more effective than concentration training at improving memory for those with an ABI.

There is level 2 evidence that N-back training compared to virtual search training is not effective for improving memory in those with an ABI.

There is level 4 evidence that Cognitive Pragmatic Treatment, Cogmed QM, and RehaCom software may improve memory and cognitive function in those with an ABI.

There is level 2 evidence that participation in a goals training program, followed by an educational program, may be more effective for improving memory in post ABI individuals compared to receiving the treatment conditions in reverse order.

There is level 2 evidence that finger sequence training, compared to no training, may not be effective for improving memory following an ABI.

There is level 1b evidence that compensatory memory strategies, self-awareness training, and participation in memory group sessions may be effective for improving memory in post ABI individuals compared to no treatment.

There is level 2 evidence that general memory rehabilitation programs are effective, compared to standard therapy, at improving memory for those with an ABI.

There is level 2 evidence that the Intensive Neurorehabilitation Programme is not effective for improving memory compared to controls in those with an ABI.

There is level 2 evidence that both computer-administered and therapist-administered memory training may be more effective than no treatment for improving memory in ABI participants. However, no treatment appears to be better than the other.

There is level 2 evidence that both cognitive remediation and emotional self-regulation may be effective at improving different elements of memory in individuals post ABI.

There is level 2 evidence that non-specific computer-based memory retraining compared, self-paced or otherwise, may not be effective at improving memory in those with an ABI.

There is conflicting level 1b evidence as to whether or not attention training programs may be effective for improving memory compared to no therapy, but positive level 1b evidence that it is not more effective than memory training programs.

There is level 2 evidence that BrainHQ is not an effective program for improving memory and learning compared to no intervention in individuals post ABI.

There is level 4 evidence that using mental representations and role-playing may not be effective at improving memory in individuals post ABI.

There is level 4 evidence that Cogmed training software may improve working memory performance and occupational performance in individuals post ABI.

There is conflicting (level 4) evidence regarding whether or not Parrot software is effective at improving memory and learning in individuals post ABI.

There is level 4 evidence that mental addition tasks may improve working memory in individuals post ABI.

There is level 4 evidence that the Wilson's Structured Behavioral Memory Program is not effective for improving memory post ABI.

There is level 1b evidence that cranial electrotherapy stimulation may not improve memory and recall compared to sham stimulation post TBI.

There is level 1b evidence that donepezil improves short-term memory compared to placebo post ABI.

There is level 4 evidence that donepezil may be effective in improving short-term, long-term, verbal, and visual memory post ABI.

There is level 1b evidence that methylphenidate compared to placebo is not effective for improving memory following brain injury for post TBI patients.

There is level 1b evidence that sertraline may not improve memory compared to placebo in individuals who have sustained a moderate to severe TBI.

There is level 1b evidence that amantadine does not improve learning and memory deficits in patients post ABI.

There is level 2 evidence that pramiracetam may improve males' memory compared to placebo post TBI.

There is level 1b evidence that oral physostigmine may improve long-term memory compared to placebo in men with TBI, however more recent studies are required.

There is level 2 evidence that bromocriptine may improve verbal memory in individuals with an ABI, however, more studies are required.

There is level 4 evidence that cerebrolysin may improve memory function post ABI.

There is level 1b evidence that recombinant human Growth Hormone (rhGH) is similar to placebo for improving memory and learning in patients post TBI.

There is level 2 evidence that growth hormone (GH) therapy is similar to placebo at improving memory ability in patients post TBI.

There is level 1a evidence that rivastigmine is not effective when compared to placebo for improving memory in ABI populations.

There is level 4 evidence that hyperbaric oxygen therapy may improve memory following an ABI.

There is level 1b evidence that targeted hypnosis may transiently improve cognitive function in post TBI patients or stroke.

There is level 1b evidence that an attention remediation intervention may not be superior to TBI education alone and improving executive function in patients post TBI.

There is level 2 evidence that dual-task training may improve not general cognitive functioning compared to a non-specific cognitive program in patients post TBI.

There is level 1b evidence that a comprehensive cognitive treatment strategy programs (which include problem solving), compared to controls, are effective for improving metacognition and goal achievement post TBI.

There is level 4 evidence that cognitive rehabilitation may increase productivity in everyday functioning, and cerebral blood flow during treatment in patients post TBI.

There is level 1b evidence that virtual-reality training is not superior to conventional cognitive training at improving cognitive and executive function outcomes post TBI.

There is level 1b evidence that the specific cognitive training program ProSolv, compared to standard therapy, does not improve measures of executive functioning following an ABI.

There is level 2 evidence that the Intensive NeuroRehabilitation programme, compared to no treatment, does not improve executive functioning following an ABI.

There is level 2 evidence that computer or smartphone software programs, such as BrainHQ, Parrot Software, ProSolv app, may not be superior to no intervention at improving problem-solving skills and general functioning in patients post TBI.

There is level 4 evidence that heart rate biofeedback may improve executive functioning following an ABI, although higher level studies are required to fully determine this.

There is level 2 evidence that goal management training may be superior (compared to motor skills training or no treatment controls) for improving goal attainment or measures of intelligence following an ABI.

There is level 1b evidence that goal orientated group interventions are successful at improving cognitive and executive function in patients post ABI.

There is level 1b evidence that emotional regulation group interventions are effective at improving executive function in post TBI patients compared to standard therapy.

There is level 1b evidence that the Strategic Memory and Reasoning Training program is more effective than a brain health workshop for improving executive function, metacognition, and comprehension following ABI.

There is level 4 evidence that metacognitive strategy instruction may not be effective for improving executive functioning following an ABI.

There is level 4 evidence that touch screen-based games (which include components of reasoning and problem-solving) may be effective for improving self-awareness and social skills following an ABI.

There is level 1b evidence that cognitive therapies compared to standard therapy are more effective than no therapy for improving generalized cognitive functioning, as well as self-perception following an ABI.

There is level 4 evidence that a low intensity outpatient cognitive rehabilitation program may improve goal attainment and cognitive impairment in patients post ABI.

There is level 2 evidence that the Trabajadora de Salud program may improve general cognitive functioning compared to standard therapy for those with an ABI.

There is level 1b evidence that corrective video feedback is more effective for improving generalized cognitive functioning and self awareness compared to verbal feedback only in those with an ABI.

There is level 1b evidence that remedial occupational therapy and adaptive occupational therapy may have equal effects on generalized cognitive function in those with an ABI.

There is level 4 evidence that mindfulness-based stress reduction may be effective for improving general cognitive functioning and psychological health for those with an ABI.

There is level 4 evidence that donepezil is effective in improving learning, memory, divided attention, and executive function in patients post TBI.

There is conflicting (level 1a) evidence regarding the effectiveness of the administration of methylphenidate, compared to placebo, following TBI for the improvement of general and executive functioning.

There is level 1b evidence that sertraline does not improve cognitive functioning, compared to placebo, in individuals who have sustained a moderate to severe TBI.

There is level 1b evidence that Amantadine may not help to improve general functioning deficits in post TBI patients compared to placebo.

There is conflicting level 2 (against) and level 4 (for) evidence as to whether or not bromocriptine may improve executive or general cognitive functioning following ABI.

There is level 1b evidence that recombinant human Growth Hormone (rhGH) is superior to placebo at improving processing speed (6 months), executive function and learning in patients post TBI.

There is level 2 evidence that growth hormone (GH) therapy is effective for improving quality of life, instrumental activities of daily living (iADL), attention, memory, and visuospatial ability in patients post TBI.

There is level 2 evidence that recombinant human Growth Hormone (rhGH) administration improves intelligence and other cognitive subtests in TBI patients with growth hormone deficiency compared to TBI patients without; however, insulin-like growth factor-1 (IGF-1) levels may be the same between groups.

There is level 1b evidence that rivastigmine is not effective for improving general or executive cognitive functioning, compared to placebo, following an ABI.

There is level 4 evidence that hyperbaric oxygen therapy may improve general and executive functioning following an ABI.

There is level 1b evidence that dextroamphetamine is not effective for the remediation of general cognitive functioning following an ABI.

There is level 1b evidence that yes/no training and an enriched environment does not significantly improve communication responses in individuals with an ABI.

There is level 4 evidence that retrieval practice is more effective for memory recall in individuals with an ABI than massed restudy (i.e., cramming) and spaced restudy (i.e., distributed learning).

There is level 4 evidence that targeted therapy towards figurative language improves communication in chronic TBI individuals.

There is level 4 evidence that text-to-speech technology improves reading rates post ABI but not reading comprehension.

There is level 4 evidence that cognitive-communication therapy targeting the interpretation of figurative language is effective for improving language and metaphor comprehension following an ABI.

There is level 1b evidence that the Social Cognition and Emotion Regulation protocol when administered by a neuropsychologist is more effective for the remediation of social communication skills than the Cogniplus protocol in individuals with an ABI.

There is level 1b evidence that a variety of communication skills training programs improve social communication skills in individuals with an ABI, as well as self-concept and self-confidence in social communications.

There is level 4 evidence suggesting that a goal-driven, metacognitive approach to intervention may be beneficial in assisting individuals with TBI to achieve social communication goals.

There is level 4 evidence that interactive touch screen games focused on areas of reasoning, knowledge and action may be effective for improving social skills following an ABI.

There is level 2 evidence that the Group Interactive Structured Treatment program (GIST) is effective for improving social communication skills in those with a TBI as well as other neuropsychological comorbidities.

There is level 2 evidence to support the effectiveness of interventions that focus on training communication partners in the community, compared to no training, for improving interactions between responders and those with an ABI.

There is level 2 evidence that providing training to both the communication partner and the individual with a TBI together is more effective than only training the individual with TBI alone or no training at all.

There is level 1b evidence that facial affect recognition training and emotional inference training is beneficial at improving the emotional perception of individuals with ABI.

There is level 1a evidence that the Treatment for Impairments in Social Cognition and Emotion Regulation and Cogniplus protocols are effective for improving emotional processing and emotional intelligence in individuals with an ABI.

There is level 1b evidence that short intervention designed to improve the ability to recognize emotional prosody was minimally effective in individuals with ABI.

There is level 4 evidence that a Cognitive Pragmatic Treatment (CPT) program is effective in improving communicative-pragmatic abilities in individuals with ABI.

6.8 References

Alvarez, X. A., Sampedro, C., Perez, P., Laredo, M., Couceiro, V., Hernandez, A., . . . Moessler, H. (2003). Positive effects of cerebrolysin on electroencephalogram slowing, cognition and clinical outcome in patients with postacute traumatic Brain Injury: an exploratory study. International Clinical Psychopharmacology, 18(5), 271-278.

American Speech-Language-Hearing Association. (1987). The role of speech-language pathologists in the habilitation and rehabilitation of cognitively impaired individuals: a Report of the Subcommittee on Language and Cognition (0001-2475 (Print) 0001-2475).

Amos, A. (2002). Remediating deficits of switching attention in patients with acquired Brain Injury. Brain Injury, 16(5), 407-413.

Arciniegas, D. B. (2003). The cholinergic hypothesis of cognitive impairment caused by traumatic Brain Injury. Current Psychiatry Report, 5(5), 391-399.

Aronow, H. U. (1987). Rehabilitation effectiveness with severe Brain Injury: Translating research into policy. Journal of Head Trauma Rehabilitation, 2(3), 24-36.

Azouvi, P., Couillet, J., Leclercq, M., Martin, Y., Asloun, S., & Rousseaux, M. (2004). Divided attention and mental effort after severe traumatic Brain Injury. Neuropsychologia, 42(9), 1260-1268.

Banos, J. H., Novack, T. A., Brunner, R., Renfroe, S., Lin, H. Y., & Meythaler, J. (2010). Impact of early administration of sertraline on cognitive and behavioral recovery in the first year after moderate to severe traumatic Brain Injury. Journal of Head Trauma Rehabilitation, 25(5), 357-361.

Barreca, S., Velikonja, D., Brown, L., Williams, L., Davis, L., & Sigouin, C. S. (2003). Evaluation of the effectiveness of two clinical training procedures to elicit yes/no responses from patients with a severe acquired Brain Injury: a randomized single-subject design. Brain Injury, 17(12), 1065-1075.

Behn, N., Togher, L., Power, E., & Heard, R. (2012). Evaluating communication training for paid carers of people with traumatic Brain Injury. Brain Injury, 26(13-14), 1702-1715.

Berg, I. J., Koning-Haanstra, M., & Deelman, B. G. (1991). Long-term effects of memory rehabilitation: A controlled study. Neuropsychological Rehabilitation, 1(2), 97-111.

Bergquist, T., Gehl, C., Mandrekar, J., Lepore, S., Hanna, S., Osten, A., & Beaulieu, W. (2009). The effect of internet-based cognitive rehabilitation in persons with memory impairments after severe traumatic Brain Injury. Brain Injury, 23(10), 790-799.

Bhatnagar SC, & F, S. (1999). Communicating with nonverbal patients in India: Inexpensive augmentative communication devices. Retrieved from http://www.dinf.ne.jp/doc/english/asia/resource/apdrj/z13jo0400/z13jo0405.html

Bloom, L., & Lahey, M. (1978). Language development and language disorders. New York: Wiley.

Boman, I. L., Lindstedt, M., Hemmingsson, H., & Bartfai, A. (2004). Cognitive training in home environment. Brain Injury, 18(10), 985-995.

Bond, F., & Godfrey, H. P. (1997). Conversation with traumatically brain-injured individuals: a controlled study of behavioural changes and their impact. Brain Injury, 11(5), 319-329.

Bondanelli, M., Ambrosio, M. R., Cavazzini, L., Bertocchi, A., Zatelli, M. C., Carli, A., . . . Uberti, E. C. (2007). Anterior pituitary function may predict functional and cognitive outcome in patients with traumatic Brain Injury undergoing rehabilitation. Journal of Neurotrauma, 24(11), 1687-1697.

Borgestig, M., Sandqvist, J., Parsons, R., Falkmer, T., & Hemmingsson, H. (2016). Eye gaze performance for children with severe physical impairments using gaze-based assistive technology: a longitudinal study. Assistive technology, 28(2), 93.

Bosco, F. M., Parola, A., Angeleri, R., Galetto, V., Zettin, M., & Gabbatore, I. (2018a). Improvement of communication skills after traumatic Brain Injury: The efficacy of the cognitive pragmatic treatment program using the communicative activities of daily living. Archives of Clinical Neuropsychology, 33(7), 875-888.

Bosco, F. M., Parola, A., Angeleri, R., Galetto, V., Zettin, M., & Gabbatore, I. (2018b). Improvement of Communication Skills after Traumatic Brain Injury: The Efficacy of the Cognitive Pragmatic Treatment Program using the Communicative Activities of Daily Living. Archives of Clinical Neuropsychology, 33(7), 875-888.

Bourgeois, M., Dijkstra, K., Burgio, L., & Allen-Burge, R. (2001). Memory aids as an augmentative and alternative communication strategy for nursing home residents with dementia. Augmentative and Alternative Communication, 17(3), 196-210.

Bourgeois, M. S., Dijkstra, K., Burgio, L., & Allen-Burge, R. (2001). Memory aids as an augmentative and alternative communication strategy for nursing home residents with dementia. AAC: Augmentative and Alternative Communication, 17(3), 196-210.

Bourgeois, M. S., Lenius, K., Turkstra, L., & Camp, C. (2007). The effects of cognitive teletherapy on reported everyday memory behaviours of persons with chronic traumatic Brain Injury. Brain Injury, 21(12), 1245-1257.

Braden, C., Hawley, L., Newman, J., Morey, C., Gerber, D., & Harrison-Felix, C. (2010). Social communication skills group treatment: a feasibility study for persons with traumatic Brain Injury and comorbid conditions. Brain Injury, 24(11), 1298-1310.

Brownell, H., Lundgren, K., Cayer-Meade, C., Milione, J., Katz, D. I., & Kearns, K. (2013). Treatment of metaphor interpretation deficits subsequent to traumatic Brain Injury. The Journal of Head Trauma Rehabilitation, 28(6), 446-452.

Burke, D. T., Leeb, S. B., Hinman, R. T., Lupton, E. C., Burke, J., Schneider, J. C., . . . Kanoalani Mayer, E. A. (2001). Using talking lights to assist brain-injured patients with daily inpatient therapeutic schedule. Journal of Head Trauma Rehabilitation, 16(3), 284-291.

Burke, R., Beukelman, D. R., & Hux, K. (2004). Accuracy, efficiency and preferences of survivors of traumatic Brain Injury when using three organization strategies to retrieve words. Brain Injury, 18(5), 497-507.

Cacabelos, R. (2007). Donepezil in Alzheimer’s disease: From conventional trials to pharmacogenetics. Neuropsychiatr Disorders and Treatment, 3(3), 303-333.

Campbell, K. A., Kennedy, R. E., Brunner, R. C., Hollis, S. D., Lumsden, R. A., & Novack, T. A. (2018). The effect of donepezil on the cognitive ability early in the course of recovery from traumatic Brain Injury. Brain Injury, 32(8), 972-979.

Cantor, J., Ashman, T., Dams-O'Connor, K., Dijkers, M. P., Gordon, W., Spielman, L., . . . Oswald, J. (2014). Evaluation of the short-term executive plus intervention for executive dysfunction after traumatic Brain Injury: a randomized controlled trial with minimization. Archives of Physical Medicine Rehabilitation, 95(1), 1-9.e3.

Canty, A. L., Fleming, J., Patterson, F., Green, H. J., Man, D., & Shum, D. H. K. (2014). Evaluation of a virtual reality prospective memory task for use with individuals with severe traumatic Brain Injury. Neuropsychology Rehabilitation, 24(2), 238-265.

Cappa, S. F., Benke, T., Clarke, S., Rossi, B., Stemmer, B., & van Heugten, C. M. (2005). EFNS guidelines on cognitive rehabilitation: report of an EFNS task force. European Journal of Neurology, 12(9), 665-680.

Cardenas, D. D., McLean, A., Jr., Farrell-Roberts, L., Baker, L., Brooke, M., & Haselkorn, J. (1994). Oral physostigmine and impaired memory in adults with Brain Injury. Brain Injury, 8(7), 579-587.

Chen, A. J., Novakovic-Agopian, T., Nycum, T. J., Song, S., Turner, G. R., Hills, N. K., . . . D'Esposito, M. (2011). Training of goal-directed attention regulation enhances control over neural processing for individuals with Brain Injury. Brain, 134(Pt 5), 1541-1554.

Chen, S. H., Thomas, J. D., Glueckauf, R. L., & Bracy, O. L. (1997). The effectiveness of computer-assisted cognitive rehabilitation for persons with traumatic Brain Injury. Brain Injury, 11(3), 197-209.

Chiaravalloti, N. D., Sandry, J., Moore, N. B., & DeLuca, J. (2016). An RCT to Treat Learning Impairment in Traumatic Brain Injury: The TBI-MEM Trial. Neurorehabilitation and Neural Repair, 30(6), 539-550.

Cicerone, K. D. (2002). Remediation of "working attention" in mild traumatic Brain Injury. Brain Injury, 16(3), 185-195.

Cicerone, K. D., Dahlberg, C., Kalmar, K., Langenbahn, D. M., Malec, J. F., Bergquist, T. F., . . . Morse, P. A. (2000). Evidence-based cognitive rehabilitation: recommendations for clinical practice. Archives of Physical Medicine and Rehabilitation, 81(12), 1596-1615.

Cicerone, K. D., Dahlberg, C., Malec, J. F., Langenbahn, D. M., Felicetti, T., Kneipp, S., . . . Catanese, J. (2005). Evidence-based cognitive rehabilitation: updated review of the literature from 1998 through 2002. Archives of Physical Medicine and Rehabilitation, 86(8), 1681-1692.

Cicerone, K. D., Langenbahn, D. M., Braden, C., Malec, J. F., Kalmar, K., Fraas, M., . . . Ashman, T. (2011). Evidence-based cognitive rehabilitation: updated review of the literature from 2003 through 2008. Archives of Physical Medicine and Rehabilitation, 92(4), 519-530.

Coelho, C. A., DeRuyter, F., & Stein, M. (1996). Treatment efficacy: cognitive-communicative disorders resulting from traumatic Brain Injury in adults. Journal of Speech and Hearing Research, 39(5), S5-17.

College of Audiologists and Speech Language Pathologists of Ontario. (2002). Preferred practice guideline for cognitive-communication disorders. Retrieved from http://www.caslpo.com/Portals/0/ppg/ppg_ccd.pdf

Combs, M. A., Critchfield, E. A., & Soble, J. R. (2018). Relax while you rehabilitate: A pilot study integrating a novel, yoga-based mindfulness group intervention into a residential military Brain Injury rehabilitation program. Rehabilitative Psychology, 63(2), 182-193.

Constantinidou, F., Thomas, R. D., & Robinson, L. (2008). Benefits of categorization training in patients with traumatic Brain Injury during post-acute rehabilitation: additional evidence from a randomized controlled trial. The Journal of Head Trauma Rehabilitation, 23(5), 312-328.

Copley, A., Smith, K., Savill, K., & Finch, E. (2015). Does metacognitive strategy instruction improve impaired receptive cognitive-communication skills following acquired Brain Injury? Brain Injury, 29(11), 1309-1316.

Couillet, J., Soury, S., Lebornec, G., Asloun, S., Joseph, P. A., Mazaux, J. M., & Azouvi, P. (2010). Rehabilitation of divided attention after severe traumatic Brain Injury: a randomised trial. Neuropsychological Rehabilitation, 20(3), 321-339.

Dahdah, M. N., Bennett, M., Prajapati, P., Parsons, T. D., Sullivan, E., & Driver, S. (2017). Application of virtual environments in a multi-disciplinary day neurorehabilitation program to improve executive functioning using the Stroop task. NeuroRehabilitation, 41(4), 721-734.

Dahlberg, C. A., Cusick, C. P., Hawley, L. A., Newman, J. K., Morey, C. E., Harrison-Felix, C. L., & Whiteneck, G. G. (2007). Treatment Efficacy of Social Communication Skills Training After Traumatic Brain Injury: A Randomized Treatment and Deferred Treatment Controlled Trial. Archives of Physical Medicine and Rehabilitation, 88(12), 1561-1573.

de Joode, E., Proot, I., Slegers, K., van Heugten, C., Verhey, F., & van Boxtel, M. (2012). The use of standard calendar software by individuals with acquired Brain Injury and cognitive complaints: a mixed methods study. Disability and Rehabilitation: Assistive Technology, 7(5), 389-398.

De Joode, E. A., Van Heugten, C. M., Verhey, F. R. J., & Van Boxtel, M. P. J. (2013). Effectiveness of an electronic cognitive aid in patients with acquired Brain Injury: A multicentre randomised parallel-group study. Neuropsychological Rehabilitation, 23(1), 133-156.

DePompei, R., & Williams, J. (1994). Working with families after TBI: A family-centered approach. Topics in Language Disorders, 15(1), 68-81.

Dirette, D. K., Hinojosa, J., & Carnevale, G. J. (1999). Comparison of remedial and compensatory interventions for adults with acquired Brain Injuryuries. Journal of Head Trauma Rehabilitation, 14(6), 595-601.

Dockree, P. M., Bellgrove, M. A., O'Keeffe, F. M., Moloney, P., Aimola, L., Carton, S., & Robertson, I. H. (2006). Sustained attention in traumatic Brain Injury (TBI) and healthy controls: enhanced sensitivity with dual-task load. Exp Brain Res, 168(1-2), 218-229.

Dou, Z. L., Man, D. W., Ou, H. N., Zheng, J. L., & Tam, S. F. (2006). Computerized errorless learning-based memory rehabilitation for Chinese patients with Brain Injury: a preliminary quasi-experimental clinical design study. Brain Injury, 20(3), 219-225.

Dowds, M. M., Lee, P. H., Sheer, J. B., O'Neil-Pirozzi, T. M., Xenopoulos-Oddsson, A., Goldstein, R., . . . Glenn, M. B. (2011). Electronic reminding technology following traumatic Brain Injury: effects on timely task completion. Journal of Head Trauma Rehabilitation, 26(5), 339-347.

Duffy, J. (2005). Defining, understanding and categorizing motor speech disorder. . In Motor speech disorders - substrates differential diagnosis, and management. (2nd ed., pp. 3-16). St. Louis, MO: Elseiver Mosby.

Dundon, N. M., Dockree, S. P., Buckley, V., Merriman, N., Carton, M., Clarke, S., . . . Dockree, P. M. (2015). Impaired auditory selective attention ameliorated by cognitive training with graded exposure to noise in patients with traumatic Brain Injury. Neuropsychologia, 75, 74-87.

Dvorkin, A. Y., Ramaiya, M., Larson, E. B., Zollman, F. S., Hsu, N., Pacini, S., . . . Patton, J. L. (2013). A "virtually minimal" visuo-haptic training of attention in severe traumatic Brain Injury. Journal of Neuroengineering Rehabilitation, 10, 92.

Dymowski, A. R., Owens, J. A., Ponsford, J. L., & Willmott, C. (2015). Speed of processing and strategic control of attention after traumatic Brain Injury. J Clin Exp Neuropsychol, 37(10), 1024-1035.

Dymowski, A. R., Ponsford, J. L., Owens, J. A., Olver, J. H., Ponsford, M., & Willmott, C. (2017). The efficacy and safety of extended-release methylphenidate following traumatic Brain Injury: a randomised controlled pilot study. Clinical Rehabilitation, 31(6), 733-741.

Eakman, A. M., & Nelson, D. L. (2001). The Effect of Hands-On Occupation on Recall Memory in Men with Traumatic Brain Injuryuries. The Occupational Therapy Journal of Research, 21(2), 109-114.

Evald, L. (2015). Prospective memory rehabilitation using smartphones in patients with TBI: What do participants report? Neuropsychological Rehabilitation, 25(2), 283-297.

Evald, L. (2018). Prospective memory rehabilitation using smartphones in patients with TBI. Disability Rehabilitation, 40(19), 2250-2259.

Fager, S., Hux, K., Beukelman, D. R., & Karantounis, R. (2006). Augmentative and alternative communication use and acceptance by adults with traumatic Brain Injury. Augment Alternative Communication, 22(1), 37-47.

Fasotti, L., Kovacs, F., Eling, P. A. T. M., & Brouwer, W. H. (2000). Time Pressure Management as a Compensatory Strategy Training after Closed Head Injury. Neuropsychological Rehabilitation, 10(1), 47-65.
Fernández, E., Bringas, M. L., Salazar, S., Rodríguez, D., García, M. E., & Torres, M. (2012). Clinical impact of RehaCom software for cognitive rehabilitation of patients with acquired Brain Injury. MEDICC review, 14(4), 32-35.
Finch, E., Cornwell, P., Copley, A., Doig, E., & Fleming, J. (2017). Remediation of social communication impairments following traumatic Brain Injury using metacognitive strategy intervention: a pilot study. Brain Injury, 31(13-14), 1830-1839.
Fish, J., Evans, J. J., Nimmo, M., Martin, E., Kersel, D., Bateman, A., . . . Manly, T. (2007). Rehabilitation of executive dysfunction following Brain Injury: "content-free" cueing improves everyday prospective memory performance. Neuropsychologia, 45(6), 1318-1330.
Foley, J. A., Cantagallo, A., Della Sala, S., & Logie, R. H. (2010). Dual task performance and post traumatic Brain Injury. Brain Injury, 24(6), 851-858.
Gabbatore, I., Sacco, K., Angeleri, R., Zettin, M., Bara, B. G., & Bosco, F. M. (2015). Cognitive Pragmatic Treatment: A rehabilitative program for traumatic Brain Injury individuals. The Journal of Head Trauma Rehabilitation, 30(5), E14-E28.
Gabbatore, I., Sacco, K., Angeleri, R., Zettin, M., Bara, B. G., & Bosco, F. M. (2015). Cognitive Pragmatic Treatment: A Rehabilitative Program for Traumatic Brain Injury Individuals. Journal of Head Trauma Rehabilitation, 30(5), E14-28.
Gentry, T., Wallace, J., Kvarfordt, C., & Lynch, K. B. (2008). Personal digital assistants as cognitive aids for individuals with severe traumatic Brain Injury: a community-based trial. Brain Injury, 22(1), 19-24.
Gerber, L. H., Narber, C. G., Vishnoi, N., Johnson, S. L., Chan, L., & Duric, Z. (2014). The feasibility of using haptic devices to engage people with chronic traumatic Brain Injury in virtual 3D functional tasks. J Neuroeng Rehabil, 11, 117.
Girolametto, L., Verbey, M., & Tannock, R. (1994). Improving Joint Engagement in Parent-Child Interaction An Intervention Study. Journal of Early Intervention, 18(2), 155-167.
Glenn, M. B. (1998). Methylphenidate for cognitive and behavioral dysfunction after traumatic Brain Injury. Journal of Head Trauma Rehabilitation, 13(5), 87-90.
Gocheva, V., Hund-Georgiadis, M., & Hediger, K. (2018). Effects of animal-assisted therapy on concentration and attention span in patients with acquired Brain Injury: A randomized controlled trial. Neuropsychology, 32(1), 54-64.
Godfrey, J. (2009). Safety of therapeutic methylphenidate in adults: a systematic review of the evidence. Journal of Psychopharmacology, 23(2), 194-205.
Gordon, W. A., Zafonte, R., Cicerone, K., Cantor, J., Brown, M., Lombard, L., . . . Chandna, T. (2006). Traumatic Brain Injury rehabilitation: state of the science. American Journal of Physical Medicine Rehabilitation, 85(4), 343-382.
Gracey, F., Fish, J. E., Greenfield, E., Bateman, A., Malley, D., Hardy, G., . . . Manly, T. (2017). A Randomized Controlled Trial of Assisted Intention Monitoring for the Rehabilitation of Executive Impairments Following Acquired Brain Injury. Neurorehabil Neural Repair, 31(4), 323-333.
Gray, J. M., Robertson, I., Pentland, B., & Anderson, S. (1992). Microcomputer-based attentional retraining after brain damage: A randomised group controlled trial. Neuropsychological Rehabilitation, 2(2), 97-115.

Grealy, M. A., Johnson, D. A., & Rushton, S. K. (1999). Improving cognitive function after Brain Injury: the use of exercise and virtual reality. Archives of Physical Medicine and Rehabilitation, 80(6), 661-667.

Greenwald, B. D., Burnett, D. M., & Miller, M. A. (2003). Congenital and acquired Brain Injury. 1. Brain Injury: epidemiology and pathophysiology. Archives of Physical Medicine and Rehabilitation, 84(3 Suppl 1), S3-7.

Grilli, M. D., & Glisky, E. L. (2013). Imagining a better memory: Self-imagination in memory-impaired patients. Clinical Psychological Science, 1(1), 93-99.

Grilli, M. D., & McFarland, C. P. (2011). Imagine that: Self-imagination improves prospective memory in memory-impaired individuals with neurological damage. Neuropsychological Rehabilitation, 21(6), 847-859.

Gualtieri, C. T., & Evans, R. W. (1988). Stimulant treatment for the neurobehavioural sequelae of traumatic Brain Injury. Brain Injury, 2(4), 273-290.

Hadanny, A., Abbott, S., Suzin, G., Bechor, Y., & Efrati, S. (2018). Effect of hyperbaric oxygen therapy on chronic neurocognitive deficits of post-traumatic Brain Injury patients: retrospective analysis. BMJ open, 8(9), e023387.

Halpern, H., Darley, F. L., & Brown, J. R. (1973). Differential language and neurologic characteristics in cerebral involvement. Journal of Speech and Hearing Disorders, 38(2), 162-173.

Hammond, F. M., Sherer, M., Malec, J. F., Zafonte, R. D., Dikmen, S., Bogner, J., . . . Temkin, N. (2018). Amantadine did not positively impact cognition in chronic traumatic Brain Injury: A multi-site, randomized, controlled trial. Journal of Neurotrauma, 35(19), 2298-2305.

Hart, T., Hawkey, K., & Whyte, J. (2002). Use of a portable voice organizer to remember therapy goals in traumatic Brain Injury rehabilitation: a within-subjects trial. Journal of Head Trauma Rehabilitation, 17(6), 556-570.

Harvey, J., Hux, K., Scott, N., & Snell, J. (2013). Text-to-speech technology effects on reading rate and comprehension by adults with traumatic Brain Injury. Brain Injury, 27(12), 1388-1394.

Hasegawa, J., & Hoshiyama, M. (2009). Attention deficits of patients with chronic-stage traumatic Brain Injury: a behavioral study involving a dual visuo-spatial task. J Clinical Experimental Neuropsychology, 31(3), 292-301.

Hellgren, L., Samuelsson, K., Lundqvist, A., & Borsbo, B. (2015). Computerized Training of Working Memory for Patients with Acquired Brain Injury. Archives of Physical Medicine and Rehabilitation, 96(10), e48-e49.

Hewitt, J., Evans, J. J., & Dritschel, B. (2006). Theory driven rehabilitation of executive functioning: improving planning skills in people with traumatic Brain Injury through the use of an autobiographical episodic memory cueing procedure. Neuropsychologia, 44(8), 1468-1474.

High, W. M., Jr., Briones-Galang, M., Clark, J. A., Gilkison, C., Mossberg, K. A., Zgaljardic, D. J., . . . Urban, R. J. (2010). Effect of growth hormone replacement therapy on cognition after traumatic Brain Injury. Journal of Neurotrauma, 27(9), 1565-1575.

Hillary, F. G., Schultheis, M. T., Challis, B. H., Millis, S. R., Carnevale, G. J., Galshi, T., & DeLuca, J. (2003). Spacing of repetitions improves learning and memory after moderate and severe TBI. Journal of Clinical Experimental Neuropsychology, 25(1), 49-58.

Holleman, M., Vink, M., Nijland, R., & Schmand, B. (2018). Effects of intensive neuropsychological rehabilitation for acquired Brain Injury. Neuropsychological Rehabilitation, 28(4), 649-662.

Holleman, M., Vink, M., Nijland, R., & Schmand, B. (2018). Effects of intensive neuropsychological rehabilitation for acquired Brain Injury. Neuropsychological Rehabilitation, 28(4), 649-662.

Iacono, T., Lyon, K., & West, D. (2011). Non-electronic communication aids for people with complex communication needs. International Journal of Speech-Language Pathology, 13(5), 399-410.

Jacoby, M., Averbuch, S., Sacher, Y., Katz, N., Weiss, P. L., & Kizony, R. (2013). Effectiveness of executive functions training within a virtual supermarket for adults with traumatic Brain Injury: a pilot study. IEEE Trans Neural Syst Rehabil Eng, 21(2), 182-190.

Jennett, S. M., & Lincoln, N. B. (1991). An evaluation of the effectiveness of group therapy for memory problems. Int Disabil Stud, 13(3), 83-86.

JL Flaubert, C. S., AM Jette. (2017). The Promise of Assistive Technology to Enhance Activity and Work Participation.: National Academies of Sciences.

Johannsen-Horbach, H., Cegla, B., Mager, U., Schempp, B., & Wallesch, C. W. (1985). Treatment of chronic global aphasia with a nonverbal communication system. Brain and Language, 24(1), 74-82.

Johansson, B., & Tornmalm, M. (2012). Working memory training for patients with acquired Brain Injury: effects in daily life. Scand J Occup Ther, 19(2), 176-183.

Jorgensen, M., & Togher, L. (2009). Narrative after traumatic Brain Injury: A comparison of monologic and jointly-produced discourse. Brain Injury, 23(9), 727-740.

Kagan, A., Black, S. E., Duchan, J. F., Simmons-Mackie, N., & Square, P. (2001). Training Volunteers as Conversation Partners Using "Supported Conversation for Adults with Aphasia" (SCA): A Controlled Trial. Journal of Speech, Language, and Hearing Research, 44(3), 624-638.

Kaschel, R., Sala, S. D., Cantagallo, A., Fahlböck, A., Laaksonen, R., & Kazen, M. (2002). Imagery mnemonics for the rehabilitation of memory: A randomised group controlled trial. Neuropsychological Rehabilitation, 12(2), 127-153.

Kelly, D. F., McArthur, D. L., Levin, H., Swimmer, S., Dusick, J. R., Cohan, P., . . . Swerdloff, R. (2006). Neurobehavioral and quality of life changes associated with growth hormone insufficiency after complicated mild, moderate, or severe traumatic Brain Injury. Journal of Neurotrauma, 23(6), 928-942.

Kennedy, M., & Deruyter, F. (1991). Cognitive and language bases for communication disorders. Communication disorders following traumatic Brain Injury: Management of cognitive, language, and motor impairments, 123-190.

Kennedy, M., & Turkstra, L. (2006). Group intervention studies in the cognitive rehabilitation of individuals with traumatic Brain Injury: Challenges faced by researchers. Neuropsychology Review, 16(4), 151-159.

Kennedy, M. R., Coelho, C., Turkstra, L., Ylvisaker, M., Moore Sohlberg, M., Yorkston, K., . . . Kan, P. F. (2008). Intervention for executive functions after traumatic Brain Injury: a systematic review, meta-analysis and clinical recommendations. Neuropsychological Rehabilitation, 18(3), 257-299.

Kennedy, M. R. T., Coelho, C., Turkstra, L., Ylvisaker, M., Moore Sohlberg, M., Yorkston, K., . . . Kan, P. F. (2008). Intervention for executive functions after traumatic Brain Injury: A systematic review, meta-analysis and clinical recommendations. Neuropsychological Rehabilitation, 18(3), 257-299.

Khateb, A., Ammann, J., Annoni, J. M., & Diserens, K. (2005). Cognition-enhancing effects of donepezil in traumatic Brain Injury. Eur Neurol, 54(1), 39-45.

Kilov, A. M., Togher, L., & Grant, S. (2009). Problem solving with friends: Discourse participation and performance of individuals with and without traumatic Brain Injury. Aphasiology, 23(5), 584-605.

Kim, H. J., Burke, D. T., Dowds, M. M., Jr., Boone, K. A., & Park, G. J. (2000). Electronic memory aids for outpatient Brain Injury: follow-up findings. Brain Injury, 14(2), 187-196.

Kim, J., Whyte, J., Patel, S., Europa, E., Wang, J., Coslett, H. B., & Detre, J. A. (2012). Methylphenidate modulates sustained attention and cortical activation in survivors of traumatic Brain Injury: a perfusion fMRI study. Psychopharmacology (Berl), 222(1), 47-57.

Kim, Y. H., Ko, M. H., Na, S. Y., Park, S. H., & Kim, K. W. (2006). Effects of single-dose methylphenidate on cognitive performance in patients with traumatic Brain Injury: a double-blind placebo-controlled study. Clinical Rehabilitation, 20(1), 24-30.

Kline, A. E., Massucci, J. L., Marion, D. W., & Dixon, C. E. (2002). Attenuation of working memory and spatial acquisition deficits after a delayed and chronic bromocriptine treatment regimen in rats subjected to traumatic Brain Injury by controlled cortical impact. Journal of Neurotrauma, 19(4), 415-425.

Korman, M., Shaklai, S., Cisamariu, K., Gal, C., Maaravi-Hesseg, R., Levy, I., . . . Sacher, Y. (2018). Atypical within-session motor procedural learning after traumatic Brain Injury but well-preserved between-session procedural memory consolidation. Frontiers in Human Neuroscience, 12, 14.

Kraus, M. F., Smith, G. S., Butters, M., Donnell, A. J., Dixon, E., Yilong, C., & Marion, D. (2005). Effects of the dopaminergic agent and NMDA receptor antagonist amantadine on cognitive function, cerebral glucose metabolism and D2 receptor availability in chronic traumatic Brain Injury: a study using positron emission tomography (PET). Brain Injury, 19(7), 471-479.

Laatsch, L., Pavel, D., Jobe, T., Lin, Q., & Quintana, J. C. (1999). Incorporation of SPECT imaging in a longitudinal cognitive rehabilitation therapy programme. Brain Injury, 13(8), 555-570.

Lannin, N., Carr, B., Allaous, J., Mackenzie, B., Falcon, A., & Tate, R. (2014). A randomized controlled trial of the effectiveness of handheld computers for improving everyday memory functioning in patients with memory impairments after acquired Brain Injury. Clinical Rehabilitation, 28(5), 470-481.

Lee, S. A., & Kim, M. K. (2018). Effect of Low Frequency Repetitive Transcranial Magnetic Stimulation on Depression and Cognition of Patients with Traumatic Brain Injury: A Randomized Controlled Trial. Med Sci Monit, 24, 8789-8794.

Lemoncello, R., Sohlberg, M. M., Fickas, S., & Prideaux, J. (2011). A randomised controlled crossover trial evaluating Television Assisted Prompting (TAP) for adults with acquired Brain Injury. Neuropsychological Rehabilitation, 21(6), 825-846.

Lennox, D. B., & Brune, P. (1993). Incidental teaching for training communication in individuals with traumatic Brain Injury. Brain Injury, 7(5), 449-454.

Lesniak, M., Polanowska, K., Seniow, J., & Czlonkowska, A. (2014). Effects of repeated anodal tDCS coupled with cognitive training for patients with severe traumatic Brain Injury: a pilot randomized controlled trial. Journal of Head Trauma Rehabilitation, 29(3), E20-29.

Leśniak, M. M., Mazurkiewicz, P., Iwański, S., Szutkowska-Hoser, J., & Seniów, J. (2018). Effects of group versus individual therapy for patients with memory disorder after an acquired Brain Injury: A randomized, controlled study. J Clin Exp Neuropsychol, 40(9), 853-864.

Levack, W. M., Siegert, R. J., Dean, S. G., & McPherson, K. M. (2009). Goal planning for adults with acquired Brain Injury: how clinicians talk about involving family. Brain Injury, 23(3), 192-202.

Levine, B., Robertson, I. H., Clare, L., Carter, G., Hong, J., Wilson, B. A., . . . Stuss, D. T. (2000). Rehabilitation of executive functioning: an experimental-clinical validation of goal management training. J Int Neuropsychol Soc, 6(3), 299-312.

Lezak, M. D. (2004). Neuropsychological assessment. New York: Oxford university press.

Li, K., Alonso, J., Chadha, N., & Pulido, J. (2015). Does Generalization Occur Following Computer-Based Cognitive Retraining?-An Exploratory Study. Occup Ther Health Care, 29(3), 283-296.

Li, K., Robertson, J., Ramos, J., & Gella, S. (2013). Computer-based cognitive retraining for adults with chronic acquired Brain Injury: a pilot study. Occup Ther Health Care, 27(4), 333-344.

Lindelov, J. K., Dall, J. O., Kristensen, C. D., Aagesen, M. H., Olsen, S. A., Snuggerud, T. R., & Sikorska, A. (2016). Training and transfer effects of N-back training for brain-injured and healthy subjects. Neuropsychological Rehabilitation, 26(5-6), 895-909.

Linton, K. F., & Kim, B. J. (2018). A pilot study of Trabajadora de salud, a lay health worker intervention for Latinas/os with traumatic Brain Injuryuries and their caregivers. Disabil Health J, 11(1), 161-164.

Llorens, R., Navarro, M. D., Alcaniz, M., & Noe, E. (2012). Therapeutic effectiveness of a virtual reality game in self-awareness after acquired Brain Injury. Stud Health Technol Inform, 181, 297-301.

MacDonald, S., & Wiseman-Hakes, C. (2010). Knowledge translation in ABI rehabilitation: A model for consolidating and applying the evidence for cognitive-communication interventions. Brain Injury, 24(3), 486-508.

Mackay, L. E., Bernstein, B. A., Chapman, P. E., Morgan, A. S., & Milazzo, L. S. (1992). Early intervention in severe head injury: Long-term benefits of a formalized program. Archives of Physical Medicine and Rehabilitation, 73(7), 635-641.

Man, D. W., Poon, W. S., & Lam, C. (2013). The effectiveness of artificial intelligent 3-D virtual reality vocational problem-solving training in enhancing employment opportunities for people with traumatic Brain Injury. Brain Injury, 27(9), 1016-1025.

Manasse, N. J., Hux, K., & Snell, J. (2005). Teaching face-name associations to survivors of traumatic Brain Injury: a sequential treatment approach. Brain Injury, 19(8), 633-641.

Masanic, C. A., Bayley, M. T., VanReekum, R., & Simard, M. (2001). Open-label study of donepezil in traumatic Brain Injury. Archives of Physical Medicine and Rehabilitation, 82(7), 896-901.

McDonald, A., Haslam, C., Yates, P., Gurr, B., Leeder, G., & Sayers, A. (2011). Google Calendar: a new memory aid to compensate for prospective memory deficits following acquired Brain Injury. Neuropsychological Rehabilitation, 21(6), 784-807.

McDonald, S., Togher, L., Tate, R., Randall, R., English, T., & Gowland, A. (2013). A randomised controlled trial evaluating a brief intervention for deficits in recognising emotional prosody following severe ABI. Neuropsychological Rehabilitation, 23(2), 267-286

McDowell, S., Whyte, J., & D'Esposito, M. (1998). Differential effect of a dopaminergic agonist on prefrontal function in traumatic Brain Injury patients. Brain, 121 (Pt 6), 1155-1164.

McHugh, L., & Wood, R. (2013). Stimulus over-selectivity in temporal Brain Injury: mindfulness as a potential intervention. Brain Injury, 27(13-14), 1595-1599.

McLean, A., Jr., Cardenas, D. D., Burgess, D., & Gamzu, E. (1991). Placebo-controlled study of pramiracetam in young males with memory and cognitive problems resulting from head injury and anoxia. Brain Injury, 5(4), 375-380.

McLean, A., Jr., Stanton, K. M., Cardenas, D. D., & Bergerud, D. B. (1987). Memory training combined with the use of oral physostigmine. Brain Injury, 1(2), 145-159.

McMillan, T., Robertson, I. H., Brock, D., & Chorlton, L. (2002). Brief mindfulness training for attentional problems after traumatic Brain Injury: A randomised control treatment trial. Neuropsychological Rehabilitation, 12(2), 117-125.

Michals, M. L., Crismon, M. L., Misko, J. S., & Childs, A. (1993). A double-blind, sham-controlled evaluation of cranial electrotherapy stimulation in posttraumatic memory impairment. The Journal of Head Trauma Rehabilitation, 8(4), 77-86.

Milders, M., Deelman, B., & Berg, I. (1998). Rehabilitation of memory for people's names. Memory, 6(1), 21-36.

Milders, M. V., Berg, I. J., & Deelman, B. G. (1995). Four-year follow-up of a controlled memory training study in closed head injured patients. Neuropsychological Rehabilitation, 5(3), 223-238.

Miller, M. A., Burnett, D. M., & McElligott, J. M. (2003). Congenital and acquired Brain Injury. 3. Rehabilitation interventions: cognitive, behavioral, and community reentry. Archives of Physical Medicine and Rehabilitation, 84(3 Suppl 1), S12-17.

Moreau, O. K., Cortet-Rudelli, C., Yollin, E., Merlen, E., Daveluy, W., & Rousseaux, M. (2013). Growth hormone replacement therapy in patients with traumatic Brain Injury. Journal of Neurotrauma, 30(11), 998-1006.

Morey, C. E., Cilo, M., Berry, J., & Cusick, C. (2003). The effect of Aricept in persons with persistent memory disorder following traumatic Brain Injury: a pilot study. Brain Injury, 17(9), 809-815.

Moseley, A. M., Herbert, R. D., Sherrington, C., & Maher, C. G. (2002a). Evidence for physiotherapy practice: A survey of the Physiotherapy Evidence Database (PEDro). Australian Journal of Physiotherapy, 48(1), 43-49.

Moseley, A. M., Herbert, R. D., Sherrington, C., & Maher, C. G. (2002b). Evidence for physiotherapy practice: a survey of the Physiotherapy Evidence Database (PEDro). Australian Journal of Physiotherapy, 48(1), 43-49.

Napolitano, E., Elovic, E. P., & Qureshi, A. I. (2005). Pharmacological stimulant treatment of neurocognitive and functional deficits after traumatic and non-traumatic Brain Injury. Medical Science Monitor, 11(6), Ra212-220.

Neistadt, M. E. (1992). Occupational therapy treatments for constructional deficits. American Journal of Occupational Therapy, 46(2), 141-148.

Neumann, D., Babbage, D. R., Zupan, B., & Willer, B. (2015). A randomized controlled trial of emotion recognition training after traumatic Brain Injury. The Journal of Head Trauma Rehabilitation, 30(3), E12-E23.

Niemann, H., Ruff, R. M., & Baser, C. A. (1990). Computer-assisted attention retraining in head-injured individuals: a controlled efficacy study of an outpatient program. J Consult Clin Psychol, 58(6), 811-817.

Novack, T. A., Caldwell, S. G., Duke, L. W., Bergquist, T. F., & Gage, R. J. (1996). Focused versus Unstructured Intervention for Attention Deficits after Traumatic Brain Injury. The Journal of Head Trauma Rehabilitation, 11(3), 52-60.

Novakovic-Agopian, T., Chen, A. J., Rome, S., Abrams, G., Castelli, H., Rossi, A., . . . D'Esposito, M. (2011). Rehabilitation of executive functioning with training in attention regulation applied to individually defined goals: a pilot study bridging theory, assessment, and treatment. Journal of Head Trauma Rehabilitation, 26(5), 325-338.

O'Neil-Pirozzi, T. M., & Hsu, H. (2016). Feasibility and benefits of computerized cognitive exercise to adults with chronic moderate-to-severe cognitive impairments following an acquired Brain Injury: A pilot study. Brain Injury, 30(13-14), 1617-1625.

O'Neil-Pirozzi, T. M., Strangman, G. E., Goldstein, R., Katz, D. I., Savage, C. R., Kelkar, K., . . . Glenn, M. B. (2010a). A controlled treatment study of internal memory strategies (I-MEMS) following traumatic Brain Injury. Journal of Head Trauma Rehabilitation, 25(1), 43-51.

O'Neil-Pirozzi, T. M., Strangman, G. E., Goldstein, R., Katz, D. I., Savage, C. R., Kelkar, K., . . . Glenn, M. B. (2010b). A controlled treatment study of internal memory strategies (I-MEMS) following traumatic Brain Injury. Journal of Head Trauma Rehabilitation, 25(1), 43-51.

O'Neill, B., Best, C., O'Neill, L., Ramos, S. D. S., & Gillespie, A. (2017). Efficacy of a Micro-Prompting Technology in Reducing Support Needed by People With Severe Acquired Brain Injury in Activities of Daily Living: A Randomized Control Trial. Journal of Head Trauma Rehabilitation.

Ownsworth, T., Fleming, J., Shum, D., Kuipers, P., & Strong, J. (2008). Comparison of individual, group and combined intervention formats in a randomized controlled trial for facilitating goal attainment and improving psychosocial function following acquired Brain Injury. Journal of Rehabilitation Medicine, 40(2), 81-88.

Ownsworth, T. L., & McFarland, K. (1999). Memory remediation in long-term acquired Brain Injury: two approaches in diary training. Brain Injury, 13(8), 605-626.

Pahisa-Solé, J., & Herrera-Joancomartí, J. (2017). Testing an AAC system that transforms pictograms into natural language with persons with cerebral palsy. Assistive technology : the official journal of RESNA, 1-9.

Parente, R., Kolakowsky-Hayner, S., Krug, K., & Wilk, C. (1999). Retraining working memory after traumatic Brain Injury. NeuroRehabilitation, 13(3), 157-163.

Parente, R., & Stapleton, M. (1999). Development of a Cognitive strategies group for vocational training after traumatic Brain Injury. NeuroRehabilitation, 13(1), 13-20.

Park, N. W. (1999). Evaluation of the Attention Process Training Programme. Neuropsychological Rehabilitation, 9(2), 135-154.

Pavlovskaya, M., Hochstein, S., Keren, O., Mordvinov, E., & Groswasser, Z. (2007). Methylphenidate effect on hemispheric attentional imbalance in patients with traumatic Brain Injury: a psychophysical study. Brain Injury, 21(5), 489-497.

Perdices, M., Schultz, R., Tate, R., McDonald, S., Togher, L., Savage, S., . . . Smith, K. (2006). The Evidence Base of Neuropsychological Rehabilitation in Acquired Brain Impairment (ABI): How Good is the Research? Brain Impairment, 7(02), 119-132.

Plenger, P. M., Dixon, C. E., Castillo, R. M., Frankowski, R. F., Yablon, S. A., & Levin, H. S. (1996). Subacute methylphenidate treatment for moderate to moderately severe traumatic Brain Injury: a preliminary double-blind placebo-controlled study. Archives of Physical Medicine and Rehabilitation, 77(6), 536-540.

Potvin, M. J., Rouleau, I., Senechal, G., & Giguere, J. F. (2011). Prospective memory rehabilitation based on visual imagery techniques. Neuropsychological Rehabilitation, 21(6), 899-924.

Powell, J. H., al-Adawi, S., Morgan, J., & Greenwood, R. J. (1996). Motivational deficits after Brain Injury: effects of bromocriptine in 11 patients. J Neurol Neurosurg Psychiatry, 60(4), 416-421.

Powell, L. E., Glang, A., Ettel, D., Todis, B., Sohlberg, M. M., & Albin, R. (2012). Systematic instruction for individuals with acquired Brain Injury: results of a randomised controlled trial. Neuropsychological Rehabilitation, 22(1), 85-112.

Quemada, J. I., Munoz Cespedes, J. M., Ezkerra, J., Ballesteros, J., Ibarra, N., & Urruticoechea, I. (2003). Outcome of memory rehabilitation in traumatic Brain Injury assessed by

neuropsychological tests and questionnaires. Journal of Head Trauma Rehabilitation, 18(6), 532-540.
Rabinowitz, A. R., & Levin, H. S. (2014). Cognitive sequelae of traumatic Brain Injury. Psychiatr Clin North Am, 37(1), 1-11.
Radice-Neumann, D., Zupan, B., Tomita, M., & Willer, B. (2009). Training emotional processing in persons with Brain Injury. Journal of Head Trauma Rehabilitation, 24(5), 313-323.
Rajaram, P., Alant, E., & Dada, S. (2012). Application of the self-generation effect to the learning of blissymbols by persons presenting with a severe aphasia. AAC: Augmentative and Alternative Communication, 28(2), 64-73.
Raskin, S. A., Buckheit, C. A., & Waxman, A. (2012). Effect of type of cue, type of response, time delay and two different ongoing tasks on prospective memory functioning after acquired Brain Injury. Neuropsychological Rehabilitation, 22(1), 40-64.
Rasquin, S. M., Bouwens, S. F., Dijcks, B., Winkens, I., Bakx, W. G., & van Heugten, C. M. (2010). Effectiveness of a low intensity outpatient cognitive rehabilitation programme for patients in the chronic phase after acquired Brain Injury. Neuropsychological Rehabilitation, 20(5), 760-777.
Rath, J. F., Simon, D., Langenbahn, D. M., Sherr, R. L., & Diller, L. (2003). Group treatment of problem-solving deficits in outpatients with traumatic Brain Injury: A randomised outcome study. Neuropsychological Rehabilitation, 13(4), 461-488.
Reimunde, P., Quintana, A., Castanon, B., Casteleiro, N., Vilarnovo, Z., Otero, A., . . . Devesa, J. (2011). Effects of growth hormone (GH) replacement and cognitive rehabilitation in patients with cognitive disorders after traumatic Brain Injury. Brain Injury, 25(1), 65-73.
Repantis, D., Schlattmann, P., Laisney, O., & Heuser, I. (2010). Modafinil and methylphenidate for neuroenhancement in healthy individuals: A systematic review. Pharmacological Research, 62(3), 187-206.
Ripich, D. N., Ziol, E., Fritsch, T., & Durand, E. J. (1999). Training Alzheimer's disease caregivers for successful communication. Clinical Gerontologist, 21(1), 37-56.
Ruff, R., Mahaffey, R., Engel, J., Farrow, C., Cox, D., & Karzmark, P. (1994). Efficacy study of THINKable in the attention and memory retraining of traumatically head-injured patients. Brain Injury, 8(1), 3-14.
Ryan, T. V., & Ruff, R. M. (1988). The efficacy of structured memory retraining in a group comparison of head trauma patients. Archives of Clinical Neuropsychology, 3(2), 165-179.
Sacco, K., Galetto, V., Dimitri, D., Geda, E., Perotti, F., Zettin, M., & Geminiani, G. C. (2016). Concomitant Use of Transcranial Direct Current Stimulation and Computer-Assisted Training for the Rehabilitation of Attention in Traumatic Brain Injuryured Patients: Behavioral and Neuroimaging Results. Frontal Behavioural Neuroscience, 10, 57.
Sandry, J., Chiou, K. S., DeLuca, J., & Chiaravalloti, N. D. (2016). Individual Differences in Working Memory Capacity Predicts Responsiveness to Memory Rehabilitation After Traumatic Brain Injury. Archives of Physical Medicine and Rehabilitation, 97(6), 1026-1029.e1021.
Sarno, M. T., Buonaguro, A., & Levita, E. (1986). Characteristics of verbal impairment in closed head injured patients. Archives of Physical Medicine and Rehabilitation, 67(6), 400-405.
Schefft, B. K., Dulay, M. F., & Fargo, J. D. (2008). The use of a self-generation memory encoding strategy to improve verbal memory and learning in patients with traumatic Brain Injury. Appl Neuropsychol, 15(1), 61-68.
Schmidt, J., Fleming, J., Ownsworth, T., & Lannin, N. A. (2013). Video feedback on functional task performance improves self-awareness after traumatic Brain Injury: a randomized controlled trial. Neurorehabil Neural Repair, 27(4), 316-324.

Schmitter-Edgecombe, M., Fahy, J. F., Whelan, J. P., & Long, C. J. (1995). Memory Remediation After Severe Closed Head Injury: Notebook Training Versus Supportive Therapy. Journal of Consulting and Clinical Psychology, 63(3), 484-489.

Schneider, W. N., Drew-Cates, J., Wong, T. M., & Dombovy, M. L. (1999). Cognitive and behavioural efficacy of amantadine in acute traumatic Brain Injury: an initial double-blind placebo-controlled study. Brain Injury, 13(11), 863-872.

Schneiderman, A. I., Braver, E. R., & Kang, H. K. (2008). Understanding sequelae of injury mechanisms and mild traumatic Brain Injury incurred during the conflicts in Iraq and Afghanistan: persistent postconcussive symptoms and posttraumatic stress disorder. Am J Epidemiol, 167(12), 1446-1452.

Schretlen, D. J., & Shapiro, A. M. (2003). A quantitative review of the effects of traumatic Brain Injury on cognitive functioning. Int Rev Psychiatry, 15(4), 341-349.

Serino, A., Ciaramelli, E., Santantonio, A. D., Malagu, S., Servadei, F., & Ladavas, E. (2007). A pilot study for rehabilitation of central executive deficits after traumatic Brain Injury. Brain Injury, 21(1), 11-19.

Shin, H., & Kim, K. (2015). Virtual reality for cognitive rehabilitation after Brain Injury: a systematic review. J Phys Ther Sci, 27(9), 2999-3002.

Shum, D., Fleming, J., Gill, H., Gullo, M. J., & Strong, J. (2011). A randomized controlled trial of prospective memory rehabilitation in adults with traumatic Brain Injury. Journal of Rehabilitation Medicine, 43(3), 216-223.

Siddiqui, S. V., Chatterjee, U., Kumar, D., Siddiqui, A., & Goyal, N. (2008). Neuropsychology of prefrontal cortex. Indian journal of psychiatry, 50(3), 202.

Sigafoos, J., & Drasgow, E. (2001). Conditional Use of Aided and Unaided AAC: A Review and Clinical Case Demonstration. Focus on Autism and Other Developmental Disabilities, 16(3), 152-161.

Silver, J. M., Koumaras, B., Chen, M., Mirski, D., Potkin, S. G., Reyes, P., . . . Gunay, I. (2006). Effects of rivastigmine on cognitive function in patients with traumatic Brain Injury. Neurology, 67(5), 748-755.

Silver, J. M., Koumaras, B., Meng, X., Potkin, S. G., Reyes, P. F., Harvey, P. D., . . . Arciniegas, D. B. (2009). Long-term effects of rivastigmine capsules in patients with traumatic Brain Injury. Brain Injury, 23(2), 123-132.

Sim, P., Power, E., & Togher, L. (2013). Describing conversations between individuals with traumatic Brain Injury (TBI) and communication partners following communication partner training: Using exchange structure analysis. Brain Injury, 27(6), 717-742.

Sisto, S. A., Forrest, G. F., & Glendinning, D. (2002). Virtual reality applications for motor rehabilitation after stroke. Top Stroke Rehabil, 8(4), 11-23.

Sohlberg, M. M., Avery, J., Kennedy, M., Ylvisaker, M., Coelho, C., Turkstra, L., & Yorkston, K. (2003b). Practice guidelines for direct attention training. Journal of Medical Speech-Language Pathology, 11(3) 343-347.

Sohlberg, M. M., McLaughlin, K. A., Pavese, A., Heidrich, A., & Posner, M. I. (2000). Evaluation of attention process training and Brain Injury education in persons with acquired Brain Injury. J Clin Exp Neuropsychol, 22(5), 656-676.

Sorita, E., N'Kaoua, B., Larrue, F., Criquillon, J., Simion, A., Sauzeon, H., . . . Mazaux, J. M. (2013). Do patients with traumatic Brain Injury learn a route in the same way in real and virtual environments? Disabil Rehabil, 35(16), 1371-1379.

Speech, T. J., Rao, S. M., Osmon, D. C., & Sperry, L. T. (1993). A double-blind controlled study of methylphenidate treatment in closed head injury. Brain Injury, 7(4), 333-338.

Spikman, J. M., Boelen, D. H., Lamberts, K. F., Brouwer, W. H., & Fasotti, L. (2010). Effects of a multifaceted treatment program for executive dysfunction after acquired Brain Injury on indications of executive functioning in daily life. J Int Neuropsychol Soc, 16(1), 118-129.

Stablum, F., Umilta, C., Mogentale, C., Carlan, M., & Guerrini, C. (2000). Rehabilitation of executive deficits in closed head injury and anterior communicating artery aneurysm patients. Psychol Res, 63(3-4), 265-278.

Story, T. B. (1991). Cognitive rehabilitation services in home and community settings. In J. S. K. P. H. Wehman (Ed.), Cognitive rehabilitation for persons with traumatic Brain Injury: A functional approach (pp. 251-267). Baltimore, MD, England: Paul H. Brookes Publishing.

Strauss HM, & RS, P. (1994). Pragmatics and treatment. . In Chapey R (Ed.), Language Intervention Strategies in Adult Aphasia. (pp. 246-268). Baltimore: Williams & Wilkins.

Struchen, M. (2005). Social communication interventions. In High W, Sander A, & H. K. (Eds.), Rehabilitation for Traumatic Brain Injury (pp. 88-117). New York, NY: Oxford University Press.

Stuss, D. T., Stethem, L. L., Hugenholtz, H., Picton, T., Pivik, J., & Richard, M. T. (1989). Reaction time after head injury: fatigue, divided and focused attention, and consistency of performance. J Neurol Neurosurg Psychiatry, 52(6), 742-748.

Sumowski, J. F., Coyne, J., Cohen, A., & Deluca, J. (2014). Retrieval practice improves memory in survivors of severe traumatic Brain Injury. Archives of Physical Medicine and Rehabilitation, 95(2), 397-400.

Sumowski, J. F., Wood, H. G., Chiaravalloti, N., Wylie, G. R., Lengenfelder, J., & DeLuca, J. (2010). Retrieval practice: a simple strategy for improving memory after traumatic Brain Injury. Journal of International Neuropsychological Society, 16(6), 1147-1150.

Tailby, R., & Haslam, C. (2003). An investigation of errorless learning in memory-impaired patients: improving the technique and clarifying theory. Neuropsychologia, 41(9), 1230-1240.

Takeda, A., Loveman, E., Clegg, A., Kirby, J., Picot, J., Payne, E., & Green, C. (2006). A systematic review of the clinical effectiveness of donepezil, rivastigmine and galantamine on cognition, quality of life and adverse events in Alzheimer's disease. International Journal of Geriatric Psychiatry, 21(1), 17-28.

Tam, S. F., & Man, W. K. (2004). Evaluating computer-assisted memory retraining programmes for people with post-head injury amnesia. Brain Injury, 18(5), 461-470.

Tenovuo, O., Alin, J., & Helenius, H. (2009). A randomized controlled trial of rivastigmine for chronic sequels of traumatic Brain Injury-What it showed and taught? Brain Injury, 23(6), 548-558.

The Mayo Clinic. (2019). Hyperbaric Oxygen Therapy. Patient Care and Health Information. Retrieved from https://www.mayoclinic.org/tests-procedures/hyperbaric-oxygen-therapy/about/pac-20394380

Thickpenny-Davis, K. L., & Barker-Collo, S. L. (2007). Evaluation of a structured group format memory rehabilitation program for adults following Brain Injury. Journal of Head Trauma Rehabilitation, 22(5), 303-313.

Thoene, A. I., & Glisky, E. L. (1995). Learning of name-face associations in memory impaired patients: a comparison of different training procedures. J Int Neuropsychol Soc, 1(1), 29-38.

Togher, L., McDonald, S., Code, C., & Grant, S. (2004). Training communication partners of people with traumatic Brain Injury: A randomised controlled trial. Aphasiology, 18(4), 313-335.

Togher, L., McDonald, S., Tate, R., Power, E., & Rietdijk, R. (2013). Training communication partners of people with severe traumatic Brain Injury improves everyday conversations: a multicenter single blind clinical trial. J Rehabil Med, 45(7), 637-645.
Togher, L., McDonald, S., Tate, R., Rietdijk, R., & Power, E. (2016). The effectiveness of social communication partner training for adults with severe chronic TBI and their families using a measure of perceived communication ability. NeuroRehabilitation, 38(3), 243-255.
Tornas, S., Lovstad, M., Solbakk, A. K., Evans, J., Endestad, T., Hol, P. K., . . . Stubberud, J. (2016). Rehabilitation of Executive Functions in Patients with Chronic Acquired Brain Injury with Goal Management Training, External Cuing, and Emotional Regulation: A Randomized Controlled Trial. Journal of International Neuropsychological Society, 22(4), 436-452.
Turkstra, L. S. (1998). The effect of stimulus presentation rate on syntax test performance in brain-injured adolescents. Aphasiology, 12(6), 421-433.
Twum, M., & Parente, R. (1994). Role of imagery and verbal labeling in the performance of paired associates tasks by persons with closed head injury. J Clin Exp Neuropsychol, 16(4), 630-639.
van den Broek, M. D., Downes, J., Johnson, Z., Dayus, B., & Hilton, N. (2000). Evaluation of an electronic memory aid in the neuropsychological rehabilitation of prospective memory deficits. Brain Injury, 14(5), 455-462.
Vas, A. K., Chapman, S. B., Cook, L. G., Elliott, A. C., & Keebler, M. (2011). Higher-order reasoning training years after traumatic Brain Injury in adults. Journal of Head Trauma Rehabilitation, 26(3), 224-239.
Waldron, B., Grimson, J., Carton, S., & Blanco-Campal, A. (2012). Effectiveness of an unmodified personal digital assistant as a compensatory strategy for prospective memory failures in adults with an ABI. Irish Journal of Psychology, 33(1), 29-42.
Walker, W., Seel, R., Gibellato, M., Lew, H., Cornis-Pop, M., Jena, T., & Silver, T. (2004). The effects of Donepezil on traumatic Brain Injury acute rehabilitation outcomes. Brain Injury, 18(8), 739-750.
Watanabe, T. K., Black, K. L., Zafonte, R. D., Millis, S. R., & Mann, N. R. (1998). Do calendars enhance posttraumatic temporal orientation?: a pilot study. Brain Injury, 12(1), 81-85.
Webb, P. M., & Glueckauf, R. L. (1994). The effects of direct involvement in goal setting on rehabilitation outcome for persons with traumatic Brain Injuryuries. Rehabil Psychol, 39(3), 179-188.
Westerhof-Evers, H. J., Visser-Keizer, A. C., Fasotti, L., Schonherr, M. C., Vink, M., van der Naalt, J., & Spikman, J. M. (2017). Effectiveness of a Treatment for Impairments in Social Cognition and Emotion Regulation (T-ScEmo) After Traumatic Brain Injury: A Randomized Controlled Trial. Journal of Head Trauma Rehabilitation, 32(5), 296-307.
Whyte, J., Hart, T., Vaccaro, M., Grieb-Neff, P., Risser, A., Polansky, M., & Coslett, H. B. (2004). Effects of methylphenidate on attention deficits after traumatic Brain Injury: a multidimensional, randomized, controlled trial. Am J Phys Med Rehabil, 83(6), 401-420.
Whyte, J., Vaccaro, M., Grieb-Neff, P., Hart, T., Polansky, M., & Coslett, H. B. (2008). The effects of bromocriptine on attention deficits after traumatic Brain Injury: a placebo-controlled pilot study. Am J Phys Med Rehabil, 87(2), 85-99.
Whyte, J. M. D. P., Hart, T. P., Schuster, K. B. S., Fleming, M. P., Polansky, M. S., & Coslett, H. B. M. D. (1997). EFFECTS OF METHYLPHENIDATE ON ATTENTIONAL FUNCTION AFTER TRAUMATIC BRAIN INJURY: A Randomized, Placebo-Controlled Trial1. American Journal of Physical Medicine & Rehabilitation November/December, 76(6), 440-450.

Wielaert, S. M., Sage, K., Heijenbrok-Kal, M. H., & Van De Sandt-Koenderman, M. W. M. E. (2016). Candidacy for conversation partner training in aphasia: findings from a Dutch implementation study. Aphasiology, 30(6), 699-718.

Willmott, C., & Ponsford, J. (2009). Efficacy of methylphenidate in the rehabilitation of attention following traumatic Brain Injury: a randomised, crossover, double blind, placebo controlled inpatient trial. J Neurol Neurosurg Psychiatry, 80(5), 552-557.

Wilson, B. A., Emslie, H., Quirk, K., Evans, J., & Watson, P. (2005). A randomized control trial to evaluate a paging system for people with traumatic Brain Injury. Brain Injury, 19(11), 891-894.

Wilson, B. A., Emslie, H. C., Quirk, K., & Evans, J. J. (2001). Reducing everyday memory and planning problems by means of a paging system: a randomised control crossover study. J Neurol Neurosurg Psychiatry, 70(4), 477-482.

Wilson, B. A., Evans, J. J., Emslie, H., & Malinek, V. (1997). Evaluation of NeuroPage: a new memory aid. J Neurol Neurosurg Psychiatry, 63(1), 113-115.

Wiseman-Hakes, C., MacDonald, S., & Keightley, M. (2010). Perspectives on evidence based practice in ABI rehabilitation. "relevant Research": Who decides? NeuroRehabilitation, 26(4), 355-368.

Wiseman-Hakes, C., Stewart, M. L., Wasserman, R., & Schuller, R. (1998). Peer group training of pragmatic skills in adolescents with acquired Brain Injury. Journal of Head Trauma Rehabilitation, 13(6), 23-36.

World Health Organization. (2001). International Classification of Functioning, Disability and Health.

Wright, P., Rogers, N., Hall, C., Wilson, B., Evans, J., & Emslie, H. (2001a). Enhancing an appointment diary on a pocket computer for use by people after Brain Injury. Int J Rehabil Res, 24(4), 299-308.

Wright, P., Rogers, N., Hall, C., Wilson, B., Evans, J., Emslie, H., & Bartram, C. (2001b). Comparison of pocket-computer memory aids for people with Brain Injury. Brain Injury, 15(9), 787-800.

Yip, B. C., & Man, D. W. (2013). Virtual reality-based prospective memory training program for people with acquired Brain Injury. NeuroRehabilitation, 32(1), 103-115.

Ylvisaker M, & SF, S. (1994). Communication Disorders Associated with Closed Head Injury. In C. R. (Ed.), Language Intervention Strategies in Adult Aphasia. (book) (pp. 546-568). Baltimore: MD: Williams & Wilkins.

Zasler ND, K. D., Zafonte RD. (2013). Brain Injury Medicine. New York: Demos Medical Publishing.

Zhang, L., Plotkin, R. C., Wang, G., Sandel, M. E., & Lee, S. (2004). Cholinergic augmentation with donepezil enhances recovery in short-term memory and sustained attention after traumatic Brain Injury. Archives of Physical Medicine and Rehabilitation, 85(7), 1050-1055.

Zhang, W. T., & Wang, Y. F. (2017). Efficacy of methylphenidate for the treatment of mental sequelae after traumatic Brain Injury. Medicine (Baltimore), 96(25), e6960.

Zickefoose, S., Hux, K., Brown, J., & Wulf, K. (2013). Let the games begin: a preliminary study using attention process training-3 and Lumosity brain games to remediate attention deficits following traumatic Brain Injury. Brain Injury, 27(6), 707-716.

Zlotowitz, S., Fallow, K., Illingworth, V., Liu, C., Greenwood, R., & Papps, B. (2010). Teaching action sequences after Brain Injury: a comparison of modelling and moulding techniques. Clinical Rehabilitation, 24(7), 632-638.