6. Cognition Interventions Post ABI

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Key Points

Specific structured training programs designed to improve attention are ineffective.

Dual-task training assists individuals in dealing with dual task situations rapidly and accurately.

Dual-task training on speed of processing is effective.

Individuals who sustained a TBI tend to perform more poorly on dual task skills.

Reaction times are slower in post-ABI individuals.

External memory aids have been shown to be an effective compensatory strategy for memory impairments.

Computer-assisted training has been shown to have a positive effect on general cognitive functioning, but has not yet been shown to be an effective treatment for the remediation of memory and attentional deficits.

Virtual reality programs may enhance the recovery of visual and verbal learning following brain injury; however more study needs to be completed as currently there is limited evidence supporting the use of VR programs.

Internal strategies appear to be an effective aid in improving recall performance.

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

Although several mnemonic strategies have been used to help improve memory post ABI, retrieval practice seems to be the most effective.

Recall and recognition of words can be enhanced by using a spaced learning condition.

Cranial electrotherapy stimulation was not shown to be an effective treatment to enhance memory and recall abilities following brain injury.
Group cognitive interventions may be effective for improving executive function; however more research needs to be completed to determine what the effectiveness is.

Goal management training is effective for treating some executive function deficits.

Programs focusing on memory strategies and selective attention post ABI have not been shown to be effective.

Outpatient day programs are effective in helping survivors of a brain injury return to competitive employment.

Donepezil helps to improve attention and short-term memory following brain injury.

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

Sertraline has not been shown to improve cognitive functioning within the first 12 months post injury.

Amantadine may not be an effective treatment to improve learning and memory deficits and executive function following brain injury.

Pramiracetam may improve memory in males.

Physostigmine improves memory in men with brain injury, but not attention, concentration, motor speed, or cognitive flexibility.

Bromocriptine improves some executive cognitive functions such as dual-task performance and motivational deficits, but it does not consistently improve memory. More research is needed before the benefits of using bromocriptine to enhance cognitive functioning are known.

Cerebrolysin may be beneficial for the improvement of cognitive functioning following brain injury.

The administration of rhGH results in improved cognitive performance in patients who been diagnosed has having a growth hormone deficiency post ABI. Due to the small sample sizes of both studies, further research with larger samples is recommended.
6. Cognition Interventions Post ABI

6.1 Remediation of Attention, Concentration & Information Processing Speed

Evaluating the efficacy of remediation or rehabilitation of attention deficits following a brain injury is complicated by a number of factors. First, there is no consensus regarding a definition of attention. Is it a general construct or does it reflect more specific subcomponents or systems of functioning (e.g., sustained, divided, focused, selective, vigilance, speed of information processing, etc)? Second, different researchers and clinicians will report using the same or similar tests to measure different aspects of attention. Third, a study may use the same outcome measures repeatedly, thereby confounding practice and treatment effects (e.g., PASAT exposure to the test). Finally, studies may not consider and account for the rate of spontaneous recovery following brain injury (i.e. would participants naturally show recovery of function in the absence of treatment?).

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. (see table 6.1)

Table 6.1 Remediation of Attentional Deficits

<table>
<thead>
<tr>
<th>Cicerone et al., (2000)</th>
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<tr>
<td>● Ethier et al., 1989</td>
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<td>● Gansler &amp; McCaffery 1991</td>
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<td>● Gray et al., 1989</td>
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<td>● Ponsford et al., 1988</td>
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<td>● Niemann et al., 1990</td>
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<td>● Novack et al., 1996</td>
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<td>● Wilson et al., 1992</td>
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<th>Cicerone et al., (2005)</th>
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<td>● Fasotti et al., 2000</td>
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<td>● Park et al., 1999</td>
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<td>● Palmese &amp; Raskin 2000</td>
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<td>● Sohlberg et al., 2000</td>
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<th>Cicerone et al., (2011)</th>
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<tr>
<td>● Coelho et al., 2005</td>
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<td>● Murray et al., 2006</td>
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<td>● Serino et al., 2007</td>
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<td>● Sohlberg et al., 2000</td>
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<td>● Tiersely et al., 2005</td>
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<td>● Westerburg et al., 2007</td>
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<td>● Vallat et al., 2005</td>
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Sinotte et al., 2007

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).

6.1.1 Drill & Practice

The following studies examined the influence of “drill & practice” exercises (either computerized and/or paper-and-pencil) on attentional functioning.

Individual Studies

Table 6.2 Influence of Drill and Practice on Attentional Functioning

<table>
<thead>
<tr>
<th>Author/Year/Country/Study design/PEDro Score</th>
<th>Methods</th>
<th>Outcome</th>
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<tr>
<td>Novack et al., (1996) USA RCT PEDro = 5</td>
<td>N=44 Individuals suffering from severe TBI, but able to communicate, were provided 30 min. of cognitive remediation five times per week in either a focused hierarchical stimulation program (attention skills) or an unstructured intervention program</td>
<td>Analysis of digit span, mental control sub-tests of WMS-R, simple &amp; choice reaction time, and functional independence revealed no significant differences in attention &amp; function skills, general cognitive abilities, or daily living activities between groups. All performed significantly better at discharge than at admission.</td>
</tr>
<tr>
<td>Park et al., (1999) Canada Case-Control</td>
<td>N=46 23 normal controls matched by age and education compared to 23 TBI subjects with attention deficits, and clinical judgment that candidate may benefit from attention process training (20 sessions / 40 hours).</td>
<td>Outcomes: Paced Auditory Serial Addition Task (PASAT), consonant trigrams, and Beck Depression inventory. Treatment (p&lt;0.01) and control (p&lt;0.001) groups improved significantly in PASAT before/after tests.</td>
</tr>
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PEDro = Physiotherapy Evidence Database rating scale score (Moseley et al., 2002)

Discussion

Novack et al. (1996) performed an RCT of severe TBI participants in acute rehabilitation and found no difference between two treatment groups “a focused group consisting of sequential, hierarchical interventions directed at specific attention mechanisms and an unstructured intervention consisting of nonsequential, nonhierarchical activities requiring memory or reasoning abilities“. No differences were found between groups in attentional, functional and/or cognitive skills assessed, although post-intervention improvement of all subjects was demonstrated as compared to pre-intervention. It
should be noted that this could reflect spontaneous recovery, as a “no-treatment”, control group was not included. Similarly, Park et al. (1999) examined whether “attention processing training (APT)” had a beneficial effect on attention measures (PASAT, Consonant Trigrams) in a severe TBI group (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 APT did not have a significantly beneficial effect as performance improved on all measures across both groups (indicating practice effects and possibly spontaneous recovery).

**Conclusion**

*There is Level 2 evidence to suggest that specific structured training programs designed to improve attention are ineffective or at best equivocal in their effects on attention.*

| Specific structured training programs designed to improve attention are ineffective. |

6.1.2 Dual-Task Training

The following studies examined the effect of “Dual-task” training on speed of processing.

**Individual Studies**

**Table 6.3 Influence of Dual-Task Training on Speed of Processing**

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<thead>
<tr>
<th>Author/Year/Country/Study design/PEDro Score</th>
<th>Methods</th>
<th>Outcome</th>
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| Couillet et al., (2010) France RCT PEDro = 5 | N=12 Each phase of the study consisted of 6 weeks of training. During this time period, participants received four 1-hour training sessions per week. The “A” of the AB/BA design referred to the control training, while the “B” referred to experimental rehabilitation. The control trainings used various cognitive tasks that did not tap on divided attention or working memory. During the experimental phase, patients were given specific dual task training. The object of the experimental treatment was to improve attention and processing speed. The outcome measures included the Digit Span subtest of the TAP (Test of\n| Following treatment, there was a significant improvement in the 2 tasks that targeted divided attention. Those who received the experimental rehab training performed better than the group who received the control training. On the digit span dual-task the BA performed significantly better than the AB group (p<0.02). Experimental training was also found to have a large effect on reaction times and omissions as reported on the divided attention subtest of the TAP (Test of
<table>
<thead>
<tr>
<th>Author/Year/Country/Study design/PEDro Score</th>
<th>Methods</th>
<th>Outcome</th>
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<tbody>
<tr>
<td><strong>Fasotti et al., (2000) Netherlands RCT</strong> PEDro = 5</td>
<td>N=22 Severe, closed TBI patients with evidence of slowed speed of information processing (assessed by PASAT, ACT, and CRT) randomized into a Time Pressure Management (TPM) treatment group (mean age: 26.1 years; chronicity 9.8 months) for 1 hour sessions 3x/week and a concentration training control group (mean age: 30.1 years, chronicity: 8.3 months) for 2-5 hrs/week over 3-4 weeks both using Waterbed (WB) and Harvard Graphics (HG) tasks. Neuropsychological tests and psychosocial questionnaires administered 2 weeks prior, at end, and 6 months following training.</td>
<td>Scores on two of three standardized memory variables and all three attention variables increased significantly in treatment group; No memory variables and 1 of 3 attention variables increased significantly for control. Follow-up data for n=10 of treatment group and n=9 of control group: pre-training follow-up showed a significant time effect (p &lt; .05) but no significant group time interaction (p = .23) indicating that there still was a significant improvement after 6 months but that this improvement could not be attributed specifically to the treatment or control group.</td>
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<tr>
<td><strong>Hasegawa &amp; Hoshiyama (2009) Case-Control</strong></td>
<td>N=54 Memory performance of TBI patients was assessed using dual visual tasks. Four sessions were developed for patients. The first and last sessions were control sessions and the two middle sessions were the experimental sessions. The experimental sessions (or the dual-task sessions) added a visual-spatial task or phonological task to the existing control sessions.</td>
<td>Overall, results indicated that the dual tasks and the memory tasks were not correlated; however, duals tasks and memory tests were correlated with the daily activity score.</td>
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<td><strong>Dockree et al., (2006) Ireland Case-Control</strong></td>
<td>N=61 Participants were asked to complete both the Sustained Attention to Response Task (SART) and the Dual Attention to Response Task (DART). This version of the DART (225 single digits from 1 to 9) was centrally presented to participants. Digits were displaced 25 times for 580 m/s, this was followed by an inter-stimulus interval of 920 m/s. Participants were asked to press a L computer mouse when any number (except 3) appeared on the screen. For the dual task they were asked</td>
<td>Performance on the SART and the DART showed those with a TBI made more errors than the control group (p&lt;0.003). Further analysis revealed that more errors were made on the DART than on the SART (p&lt;0.0001) for both groups; however, the errors made by the TBI participants, were correlated with the variability in response times and with everyday cognitive failures.</td>
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<table>
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<tr>
<th>Author/Year/Country/Study design/PEDro Score</th>
<th>Methods</th>
<th>Outcome</th>
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<tr>
<td>Stablum et al., (2000) Italy Case-Control</td>
<td>to press the L computer mouse for all numbers but 3 and the R mouse when the number appeared in grey.</td>
<td>Reaction time for closed head injury (p&lt; 0.0001) and aneurysm (p&lt; 0.007) group significantly slower than control. Closed head injury mean time significantly slower than control (p&lt; 0.012).</td>
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<tr>
<td>Foley et al., (2010) UK Case Series</td>
<td>N=38 10 closed head injured and 9 anterior communicating artery aneurysm patients with no history of previous injury, no visual/motor deficit psychiatric illness, mental retardation, alcoholism or depression with matching controls (n=19) participate in five sessions with the Paced Auditory Serial Addition Task.</td>
<td>Twenty-one out of the 86 who participated performed in the impaired range. The majority of these individuals had sustained a severe TBI. GCS and PTA did not play a role in participant performance; it in no way suggested who would perform poorly. Performance on the dual task assignments was also not linked to who performed poorly on the neuropsychological assessments. Of those who performed poorly on the dual task assessment a greater number also had deficits in emotional control and awareness.</td>
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PEDro = Physiotherapy Evidence Database rating scale score (Moseley et al., 2002).

Discussion
In a recent RCT, Couillet et al. (2010) randomly divided 12 participants into either a non-specific cognitive group that did not tap on divided attention or working memory or an experimental rehabilitation training program with specific dual task training. Six individuals were assigned to either: the control/experimental group (AB) or the experimental/control (BA) group. Prior to completing the dual task, all were asked to complete the single tasks until they were able to do so without difficulty. To measure changes in divided attention, the divided attention subtest of the TAP was used. At the 6th week assessment period the BA group showed significant improvement (p<0.01) in reaction times and omissions compared to the AB group.
Fasotti et al. (2000) randomly assigned 22 severe TBI patients undergoing rehabilitation to either Time Pressure Management (TPM) training (treatment group, N=12) or to a concentration group (control, N=10). Patients were pre-selected for inclusion in this study if they demonstrated slowed processing speed (as measured by 3 tests). TPM consists of a series of cognitive strategies to compensate for reduced processing speed. There are 3 main stages: increased self-awareness of errors and deficits, acceptance and acquisition of TPM cognitive strategies (4 steps), and strategy application and maintenance in increasingly more demanding/distracting situations. The concentration-training group consisted of 4 generic suggestions (e.g., focus, don’t get distracted, etc). Groups were compared on pre-training, post-training and follow-up on task performance (information from a video recording) and results indicated that there were no significant differences between groups (both improved task performance), although the TPM made more gains and appeared to generalize to positive effects other measures.

In a study conducted by Hasegawa and Hoshiyama (2009) patients were initially presented with visual stimuli of Japanese characters. Participants were shown one character for 3 seconds, and then 4 appeared on screen for 3 seconds. Patients were asked to identify on a piece of paper which characters (4) and the position they had on screen. Participants were expected to retain the memory for 7 seconds before they recalled it. During the experimental sessions participants were presented orally with 4 numbers which they were asked to repeat before writing down the symbols they saw on the screen. During the visual-spatial task, flicker stimulation (1 or 2 dots) randomly appeared on the screen. Participants were asked to follow the flickering lights. Following this, each participant wrote down the characters presented on the screen. The first and last sessions were control sessions and the two middle sessions were the experimental sessions. In the control and visuo-spatial task sessions, the correct answer rate was higher for the character being presented than for locations (p<0.05), in the phonological task session, the location was higher than that for character (p<0.05). When looking at the repetition effects, during the control session (session 1 and 4), the correct answer rate was higher. Results of the memory tests and the results on the various scales used indicated the RBMT and the social activity scores were correlated (r=.53, p<0.02). The dual task cost for both factors in the phonological and visuo-spatial session were negatively correlated with the social and personal activity score (r = -.43, p<0.05; r = -.42, p<.03) respectively. Overall the TBI groups showed memory disturbances in the simple memory test and RBMT; correct answer rates in the control and dual task session were all lower in the patient group compared to the control group; the correct answer rates for the TBI patients in the dual task experiment were lower than in the control group. ADLs were all highly correlated with the dual task and memory tests, but dual tasks and memory tests were not correlated.
Dockree et al. (2006) in a case control study compared the performance of individuals who had sustained a brain trauma to those that had not. All participants participated in two tasks of sustained attention: a single task of sustained attention (SART) and a dual task of sustained attention (DART). Results indicate that the TBI patients made significantly more errors (p<0.0001) than their non-TBI counterparts on the dual task sustained attention compared to the single task sustained attention.

Stablum et al. (2000) compared two patient groups (those suffering from a closed head injury (CHI) and those who experienced an aneurism of the anterior communicating artery (ACoA) and matched controls on performance on a dual-task paradigm and neuropsychological tests. Results suggested that CHI and ACoA patients had significant difficulty compared to matched controls on dual-task reaction time measure and specific measures of executive functioning (e.g., WCST and PASAT) and compared to their own performance on a single-task reaction time measures (non-significant differences between groups on this latter measure). With training, however, performance improved to levels similar to matched control subjects and was maintained at follow-up 3 months later. However, what remains unclear is whether training generalized to functional gains or whether it remained specific to this specific dual-task.

In a case series by Foley et al. (2010) they found that level of injury severity as measured by the GCS or PTA did not play a role in who performed poorly on the dual task assignment given to participants. They found that approximately 26% of the study population performed below the cut-off for normal performance. The authors concluded that fewer than expected had deficits in attentional control.

**Conclusion**

*There is Level 2 evidence that dual task training has a positive effect on divided attention.*

*There is Level 2 evidence that dual-task training is effective on the speed of processing.*

*There is Level 3 evidence that individuals with a TBI perform poorly on dual task activities due to their inability to maintain a measure of sustained attention.*

**Dual-task training assists individuals in dealing with dual task situations rapidly and accurately.**

**Dual-task training on speed of processing is effective.**
Individuals who sustained a TBI tend to perform more poorly on dual task skills.

6.1.3 Reaction Time
It has been noted that those who have sustained a severe traumatic brain injury tend to have a slower reaction time than those who have not (Stuss et al., 1989; Azouvi et al., 2004).

Individuals Studies

**Table 6.4: Reaction Time post-TBI**

<table>
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<tr>
<th>Author/Year/Country/Study Design</th>
<th>Methods</th>
<th>Results</th>
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<tr>
<td>Azouvi et al., (2004) France Case-Control</td>
<td>N=85 43 cases (TBI group) were compared to 42 healthy controls. Two different tests were conducted: In the <strong>visual go-no go task</strong>, participants (while facing a screen) were asked to respond to a target presentation by pressing a response button as soon as possible. In the <strong>random number generation</strong> test subjects were asked to say aloud a series of 100 numbers between 1 &amp; 10 in random order.</td>
<td>In both tests those with a TBI responded slightly slower then those without a TBI. Results from the VAS indicate that mental effort was higher for the cases than the controls. When looking at the task X condition interaction, mental effort in both tasks was higher under dual task condition compared to single task condition.</td>
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<td>Stuss et al., (1989) Canada Case-Control</td>
<td>N=140 In this case-control study participants, cases-those with a TBI-n=70) and controls-(those without a TBI-n=70) indicated when they saw stimuli after it appeared on a coloured monitor by pressing a button. Reaction time was recorded. Both cases and controls were divided into 3 groups, creating 3 separate studies</td>
<td>Those with a TBI had a slower reaction time than those without a TBI. For those in Group 3 this difference was significant (p&lt;0.05). Results from the multiple choice reaction time (MCRT) indicated there was a significant test difference for all 3 studies, but significant group differences were noted only for studies 1 and 2. The GCS was found to correlate significantly with the difference between the Easy and Redundant RT measures (r=-0.43 p&lt;0.01), with the more severe injuries having a greater redundancy effect.</td>
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Discussion
Two studies were found looking at the reaction times of individuals with a TBI and comparing these times with individuals who had not sustained a TBI (Stuss et al., 1989; Azouvi et al., 2004).
Azouvi et al., 2004). Both case-control studies demonstrated that those with a TBI were found to have slower reaction times. Struss et al. (1989), after conducting three studies, found (in study 3), those with a brain injury were significantly slower than the group without an injury (p<0.01) on the simple reaction time test. Results from the multiple choice reaction time (MCRT), indicated that regardless of the severity of the injury (mild concussion to severe TBI) those with a TBI had a slower reaction time than the controls. Azouvi et al. (2004) found that those with a brain injury were slower than those without when looking at the results of tasks the groups were asked to perform. 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 2 simultaneous tasks (Azouvi et al., 2004).

Conclusion

*There is Level 3 evidence that reaction times of those with a TBI are slower than the reaction times of those without.*

### 6.2 Remediation 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 or retraining of the function and compensation. Compensation includes “training strategies or techniques that aim to circumvent any difficulty that arises as a result of the memory impairment.” Compensatory techniques include internal aids, which are “mnemonic strategies that restructure information that is to be learned.” Various interventions have focused on the remediation of memory deficits in individuals with TBI, including external compensatory aids (computers, pagers, and notebooks), individualized remediation programs, family/social support and environmental adaptations, didactic lessons and homework, training in compensatory strategies including rehearsal, organizational strategies, visual imagery, verbal labeling, and use of mnemonics, as well as implicit memory tasks.
Cicerone et al. (2000) reviewed 42 studies examining the effectiveness of various interventions to improve memory impairment following stroke and TBI. In 2005 and again in 2011, Cicerone and colleagues updated their original review (Table 6.5). It should be noted that studies were not included in our review if the population did not comprise of more than 50% brain-injured patients, or if the sample size (n) was less than 3. As well only those studies dealing with moderate-to-severe brain-injured individuals were included in this review.

Cappa and colleagues (2005) reviewed various strategies used to improve memory deficits without the use of electronic, external aids were judged to be “possibly effective.” 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 impairment.

Several studies were identified examining interventions to improve learning and memory following acquired brain injury. Studies were categorized into the following groupings: assistive technology (external aids, computer assisted training and virtual reality and cognitive functioning), internal strategies used during learning to enhance recall, memory interventions and cranial electrotherapy stimulation and memory

Table 6.5 Remediation of Memory Deficits

Cicerone et al., (2000)

- Benedict et al., 1992
- Benedict et al., 1993
- Berg et al., 1991
- Burke et al., 1994
- Cancelliere et al., 1991
- Chute et al., 1988
- Crosson et al., 1984
- Evans et al., 1996
- Finset et al., 1995
- Fowler et al., 1972
- Freeman et al., 1992
- Furst et al., 1994
- Gianutsos et al., 1979
- Glasgow et al., 1977
- Godfrey et al., 1988
- Goldstein et al., 1996
- Goldstein et al., 1988
- Hersh et al., 1994
- Kim et al., 1996
- Kerner et al., 1985

Cicerone et al., (2005)

- Kirsch et al., 1987
- Kirsch et al., 1992
- Laatsch et al., 1983
- Leng et al., 1991
- Malec et al., 1983
- Malec et al., 1991
- Malloy et al., 1984
- Milders et al., 1998
- Parente et al., 1983
- Parente 1994
- Schacter et al., 1985
- Schmitter-Edgecombe et al., 1995
- Squires et al., 1996
- Raskin et al., 1996
- Ryan et al., 1988
- Sohliberg et al., 1992
- Thoene et al., 1995
- Wilson 1982
- Zencius et al., 1990
6.2.1 Assistive Technology

6.2.1.1 External Aids

External aids, of which there are active or high tech (computers, PDAs, and mobile phones) and passive or no tech/no tech (calendars, diaries, lists, timetables and dictaphones) have been shown to assist 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 several studies which examined how external aids, both active and passive, could be used to enhance memory following brain injury.

Individual Studies

Table 6.6 External Aids to Enhance Memory

<table>
<thead>
<tr>
<th>Author/Year/Country/Study design/PEDro Score</th>
<th>Methods</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Powell et al., (2012) USA RCT PEDro=7</td>
<td>N=29 Participants were randomly assigned to one of two groups, the conventional instruction group (trial and error learning, errorful learning) or the systematic instruction. The systematic instruction condition emphasized mastery, while the conventional instruction emphasized exploratory learning, not mastery. Training sessions</td>
<td>Pre-tests indicated the groups were equal prior to the introduction of the intervention. Those exposed to the intervention (systematic instruction) performed significantly more (p&lt;0.01) correct tasks at the 30 day assessment. Fluency scores (their ability to follow through with a task) were also found to increase in those in systematic instruction</td>
</tr>
</tbody>
</table>
**Methods**

- **Dowds et al., (2011)**
  - USA
  - RCT
  - PEDro=5
  - Participants were trained how to use 2 memory aids (a PDA or a paper organizer) to assist them in organizing activities that needed to be completed throughout the week.

- **McDonald et al., (2011)**
  - UK
  - RCT
  - PEDro=5
  - Participants were randomly assigned to 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.

- **Lemoncello et al., (2011)**
  - USA
  - RCT
  - PEDro=5
  - Participants were randomly assigned to either the Television Assisted Prompting (TAP) group or the Assistive Technology for Cognition (ATC) group. The TAP system was a set-top box to allow the participant to interact with the system through the television. This system delivers reminders (either text or audio-video) at pre-specified times to participants. The ATC system was individualized to meet the needs of each person.

- **Shum et al., (2011)**
  - N=45
  - Individuals were assigned to 1 of 4 treatment groups using a restricted all 4 groups showed no significant differences on the CAMPROMPT during the intervention.

**Outcome**

- **Dowds et al., (2011)**
  - Overall the use of memory aids assisted individuals in completing tasks as opposed to no memory aids. During the Google Calendar intervention phase, there was 40.6% increase in completing their prospective intention compared to the standard diary phase. Overall 82% of targets were reached using Google calendar but only 55% using the standard diary.

- **McDonald et al., (2011)**
  - When using the PDAs the individuals had a higher task completion rate than when they used paper memory aids. Results also indicated that those using the Palm OS PDA had a higher completion rate than those using the Microsoft pocket PDA.

- **Lemoncello et al., (2011)**
  - No significant differences were found between groups A or B; therefore data from the two groups was collapsed. Following this, the TAP group (n=23) had a higher task completion rate compared to their typical practice strategies. The TAP system improved task completion from 43% pre intervention to 72% post intervention.

- **Shum et al., (2011)**
  - All 4 groups showed no significant differences on the CAMPROMPT during the intervention.
<table>
<thead>
<tr>
<th>Author/Year/Country/Study design/PEDro Score</th>
<th>Methods</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Australia RCT PEDro=7</td>
<td>randomization with blocking procedure. All interventions involved 8 weekly attendances (1.5hrs each) at an individual therapy session. In total there were 4 programs, with each one compromising 2 weeks’ self awareness training or active control plus 6 weeks compensatory prospective memory (PM) training or active control. Programs included: self-awareness compensatory prospective memory training; self-awareness training plus active control; active control plus compensatory prospective memory training; and active control only.</td>
<td>pre-intervention phase. Following intervention, those with a self-awareness training component were not significantly different from those without on the change scores. Groups with a compensatory training component were found to have a significantly larger change score than those with out. Overall, the group that received self-awareness and compensatory PM training did not have the largest change score on the CAMPRMT. An assessment of the number of valid diary entries per week did not differ between the four groups pre interventions. Post intervention the groups with a compensatory training component were found to have larger change scores than those without (p&lt;0.017).</td>
</tr>
<tr>
<td>Wilson et al., (2001) UK RCT PEDro = 4</td>
<td>N=143 A randomized controlled cross-over study of subjects with memory impairments were divided into one of two treatment groups: group A (pager first) and group B (waiting list first). Patients chose their own tasks in which they wanted to be reminded. Outcomes measured included patients’ ability to successfully carry out everyday tasks.</td>
<td>During the last 2 weeks of the 7-week treatment period, the participants using the pager were significantly more successful in achieving target behaviours than the waiting list group (p&lt; 0.001).</td>
</tr>
<tr>
<td>Ownsworth &amp; McFarland (1999) Australia RCT PEDro = 3</td>
<td>N=20 Volunteer subjects with ABI were randomized into a diary only (DS) and a diary &amp; self-instructional training (DSIT) group 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.”</td>
<td>All subjects reported significantly fewer problems with memory (p&lt;0.001) and lower levels of distress (p&lt;0.01) during treatment phase when compared to baseline. There was a significant increase in the degree of strategy use during treatment (p&lt;0.05) regardless of type of diary training. There were no significant differences between the DS and DSIT groups (p&gt;0.05).</td>
</tr>
<tr>
<td>Watanabe et al., (1998) USA RCT</td>
<td>N=30 Severe TBI subjects (determined by length of PTA @ acute rehabilitation admittance) consecutively admitted to a BI inpatient unit (16 traumatic, 14 non-</td>
<td>Presence of a calendar did not significantly affect TOT scores.</td>
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<tr>
<td>Author/Year/Country/Study design/PEDro Score</td>
<td>Methods</td>
<td>Outcome</td>
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<tr>
<td>PEDro = 3</td>
<td>traumatic: without aphasia or severe visual deficits) were randomized into treatment (n=14), and control groups (n=16) to determine whether the presence of a calendar affected the score from the Temporal Orientation Test (TOT).</td>
<td>An odds ratio test revealed that 81% of the 63 patients who completed all stages of the trial were significantly more successful with the pager.</td>
</tr>
<tr>
<td>Wilson et al., (2005) UK Sub-group analysis of Wilson et al. (2001)</td>
<td>N=63 TBI subjects with memory impairments were divided into one of two treatment groups: group A (pager first) and group B (waiting list first). Patients chose their own tasks in which they wanted to be reminded. Outcomes measured included patients’ ability to successfully carry out everyday tasks.</td>
<td>This paging system helps people with memory impairments, due to TBI, document successful task achievement more efficiently than without the pager.</td>
</tr>
<tr>
<td>Bourgeois et al., (2007) USA Quasi-RCT PEDro=2</td>
<td>N=38 Individuals were quasi-randomized into either the spaced retrieval (SR) group or the didactic strategy instruction (SI) group. Daily memory logs noted areas where the participant was having difficulties and specific goals to work on were selected. 30 minute training sessions were scheduled 4 or 5 per week. Those in the SR treatment group began with a prompt question and a treatment goal. Participants were encouraged to answer the question(s) the same way each time it/they was asked. Those in the SI group common memory strategies were discussed. Participants were encouraged to identify problems and then apply a specific strategy to help deal with this problem. Contact with all participants was done over the phone.</td>
<td>The frequency of memory problems decreased in both groups over time. Those in the SR group showed significant improvement in goal mastery (p&lt;0.05) compared to the SI group. This was maintained at the one month post intervention time period. Results on the Cognitive Difficulties Questionnaire (CDS) showed both groups reported having fewer difficulties following treatment. There were no significant differences between the two groups on the CIQ post treatment. Changes in community integration were not noted over time.</td>
</tr>
<tr>
<td>Schmitter-Edgecombe et al., (1995) USA Non-RCT</td>
<td>N=8 participants with severe CHI and documented memory deficits (WAIS-R-IQ&gt;75; DRS &gt;133; WMS-R&gt;89) were matched and allocated to memory notebook training (treatment) and supportive therapy (control) groups for 9 weeks. Outcome measures assessed at baseline, after treatment and at 6-month follow-up.</td>
<td>Immediately after treatment, the notebook training group reported significantly fewer observed EMFs than the control group (p &lt; 0.05), although this finding was no longer significant at the 6-month follow-up. There were no significant differences between groups in any of the other outcomes measures (laboratory based-recall,</td>
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<tr>
<td>Author/Year/</td>
<td>Methods</td>
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</tr>
<tr>
<td>Country/Study design/PEDro Score</td>
<td>month follow-up included lab-based recall (Logical Memory I &amp; 2 scales and Visual Reproduction 1 &amp; 2 scales from the Wechsler Memory Scale – Revised), laboratory-based everyday memory tests (Rivermead Behavioural Memory Test), retrospective report of Everyday Memory Failures (EMFs) using the Everyday Memory Questionnaire (EMQ), observed EMF (EMQ assessed for 7 consecutive days), and symptom distress (Global Severity Index from the Symptom Checklist 90 – Revised).</td>
<td>laboratory-based everyday memory, retrospective report of EMFs, and symptom distress indicators).</td>
</tr>
<tr>
<td>Boman et al., (2007) Sweden Pre-Post</td>
<td>N=8 Participants were invited to move into one of 2 apartments for a period of 4 to 6 months. Apartments were equipped with electronic aids to daily living (EADLs). Learning how to use the EADLs was completed in the rehab clinic within 2-3 days. Once in the apartment participants were taught to use all the EADLs available to them. Training lasted 1-2 hours, 4 or 5 x per week for 3 weeks. Once all the EADLs were presented, time and attention were given to helping the individual use the ones needed in their everyday life. The Canadian Occupation Performance Measure (COPM) was used measure perceived improved function of everyday activities, the Sickness Impact Profile 136 (SIP-136) was used to measure self perceived dysfunction and the quality of life analogue scale was used to measure self perceived quality of life.</td>
<td>Individuals varied in the length of time (2 to 24 weeks) needed to learn how to use the EADLs. It took approximately four weeks for all to learn the very basic EADLs such as the electronic key, the photoelectric controlled water taps, etc. All felt the EADLs were very useful. Prior to beginning the study, results of the COPM indicated a lack of initiation to do what they said they would do, being on time for meetings and a decreased ability to plan things as major problems for most of the participants. During the post stage of the study, a significant improvement was noted in the self perceived ability to perform important activities and in the satisfaction with performing tasks (p&lt;0.05). For 6 participants improvement was also seen on the SIP (p&lt;0.05), in the following categories: body care, and psychosocial functioning. Overall occupational health and quality of life was found to have improved.</td>
</tr>
<tr>
<td>Egan et al., (2005) Australia Pre-Post</td>
<td>N=7 Individuals were chosen to participate in the following study although only 6 completed it. Through the help of tutors (n=6) individuals were trained one on one to use the internet.</td>
<td>The majority of participants had rarely or never used the internet although most has internet access in their homes. There was a significant improvement on the post rating of moderate to total independence on the internet skills assessment scale (p&lt;0.028). Any task that required more steps or required a greater understanding of how to</td>
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<tr>
<td>Author/Year/ Country/Study design/PEDro Score</td>
<td>Methods</td>
<td>Outcome</td>
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<tr>
<td>Hart et al., (2002) USA Pre-Post</td>
<td>N=20 TBI subjects exhibiting significant memory impairments were involved in a comprehensive treatment program 2-5 days per week. Individualized therapy goals were assigned prospectively to intervention or non-intervention groups with “memory for therapy” goals being the primary outcome.</td>
<td>use the internet showed little improvement in independence. Recorded goals were recalled significantly better than unrecorded goals.</td>
</tr>
<tr>
<td>Burke et al., (2001) USA Pre-Post</td>
<td>N=5 TBI subjects with functional hearing, vision and mobility were prompted by hospital staff about appointment times and locations verbally (baseline) or using an electronic device (Patient Locator and Minder – PLAM – treatment). Measures included the number of prompts and arrival time at baseline compared to PLAM.</td>
<td>Average number of human prompts declined significantly (p&lt;0.001), while the number of sessions requiring no prompting increased (p&lt;0.005). Patients arrived on average 1.3 minutes earlier using PLAM – a 6.1 minute improvement over baseline.</td>
</tr>
<tr>
<td>Wright et al., (2001a) UK Pre-Post</td>
<td>N=12 Subjects with ABI via TBI (9) and subarachnoid hemorrhage (2) were provided with 2 different computer aid formats for 2 months (with a one month gap between machines). Frequency of feature use, as well as the user’s willingness to use a specific feature was recorded.</td>
<td>Appointment diary was used more than any other aid. High users made more new diary entries (p&lt;0.06) suggesting a conceptual understanding of how to use memory aids in everyday living was a prerequisite for benefiting from them.</td>
</tr>
<tr>
<td>Wright et al., (2001b) UK Pre-Post</td>
<td>N=12 Adult, TBI volunteers without visual or motor handicaps that would prevent the use of an electronic organizer completed a two month comparative study of Casio and HP electronic organizers (one month break between brands).</td>
<td>No significant correlations between any single psychometric measure and organizer entries. People accustomed to using memory aids (any type) made more use of pocket computers (p&lt;0.07). Low frequency users were put off organizers when it had a physical keyboard (p&lt;0.01). High frequency users used the keyboard more (p&lt;0.07).</td>
</tr>
<tr>
<td>Wilson et al., (1997) UK Pre-Post</td>
<td>N=15 Subjects with everyday memory problems due to neurological impairment from ABI completed a study of the efficacy of the NeuroPage paging system. A diary was kept in advance to identify real-life problems for each subject that served as treatment goals. Reminders for targeted problems were sent out by pager at agreed upon times;</td>
<td>There was a significant improvement in task completion between the baseline and treatment phase of each subject (p&lt;0.05). Mean success at baseline was 37.08%, during treatment (85.56%) and post-treatment (74.46%).</td>
</tr>
<tr>
<td>Author/Year/Country/Study design/PEDro Score</td>
<td>Methods</td>
<td>Outcome</td>
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<tr>
<td>Fish et al., (2007) UK Case Series</td>
<td>Participants were asked to make telephone calls at specific times of the day for a 3 week period. 4 calls were made each day at which time the participant was asked to leave their name only. Times of the call were randomly selected each day but participants were given the times to call. Some telephone tasks were expected to be completed at a particular time, while others were given a time frame for completion. Participants were scored on the number of calls made in a day (0-4) and the time the call was made. Over the 3 week period on 5 randomly selected days a text message “STOP” was sent to participants. This was a cue for participants to stop and think about what needed to be done, what they were doing etc.</td>
<td>During the first week 15% of the participants failed to make the calls. The effect of cueing on participants had a significant impact on the number of calls made. Participants made 87.6% of calls when cued but only 71.2% of calls when they were not cued. 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).</td>
</tr>
<tr>
<td>van den Broek et al., (2000) UK Case Series</td>
<td>Outpatients of the Brain Injury Rehabilitation Centre were used to evaluate the effectiveness of the external aid, the Voice Organizer for a period of 3-weeks. This aid has a visual display presenting the current time, day and date and each device was trained to recognize the user’s voice. Messages could be dictated into the organizer and verbal reminders were repeated at specified times throughout the day.</td>
<td>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).</td>
</tr>
<tr>
<td>Manasse et al., (2005) USA Case Series</td>
<td>Subjects were shown pictures of individuals they interacted with daily and asked to identify them. Traditional treatment: To assist subjects in memory recall, pictures were paired with an imagery statement. There were 9 (3 weekly 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</td>
<td>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. Real-world treatment: During the real-world cueing condition only 2 names were consistently used by each subject. When directly asked a person’s name 4 of 5 subjects could respond correctly.</td>
</tr>
</tbody>
</table>
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.

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

Table 6.7 Summary of the Use of External Aides to Enhance Memory

<table>
<thead>
<tr>
<th>Authors</th>
<th>n</th>
<th>Intervention</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>McDonald et al., (2011)</td>
<td>12</td>
<td>Participants were taught how to use Google calendar to assist them with an prospective memory impairments they were experiencing</td>
<td>The Google calendar was found to be more effective than the traditional diary in enhancing prospective memory performance.</td>
</tr>
<tr>
<td>Lemoncello et al., (2011)</td>
<td>23</td>
<td>Subjects were randomly assigned to either the TAP or TAC group</td>
<td>Overall the TAP system improved task completion.</td>
</tr>
<tr>
<td>Powell et al., (2012)</td>
<td>29</td>
<td>Participants were randomly assigned to one of two groups, the conventional instruction group (trail and error learning, errorful learning) or the systematic instruction (ATC).</td>
<td>Those assigned to the systematic instruction group showed better skill maintenance and generalization compared to those assigned to the conventional instruction group.</td>
</tr>
<tr>
<td>Dowds et al., (2011)</td>
<td>36</td>
<td>Participant were first asked to remember various tasks using familiar methods; however during the following weeks they were asked to use either a paper-based schedule book with weekly format (a POS-based PDA or a MOS-based PDA).</td>
<td>The MOS PDA and the POS PDA were both significantly higher than the baseline condition.</td>
</tr>
<tr>
<td>Shum et al., (2011)</td>
<td>45</td>
<td>Subjects were randomized to one of 4 treatment programs.</td>
<td>Compensatory memory training programs were found to improve prospective memory test scores better than other training strategies.</td>
</tr>
<tr>
<td>Ownsworth &amp; McFarland (1999)</td>
<td>20</td>
<td>Subjects randomized to Diary Only (goal oriented strategy) and Diary and Self-Instructional Training (compensation strategy) group.</td>
<td>During treatment phase, DSIT group consistently made more entries (p&lt;0.05), reported fewer memory problems (p&lt;0.025) and made more positive ratings towards treatment efficacy.</td>
</tr>
<tr>
<td>Authors</td>
<td>n</td>
<td>Intervention</td>
<td>Result</td>
</tr>
<tr>
<td>-------------------------------</td>
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</tr>
<tr>
<td>Watanabe et al., (1998)</td>
<td>30</td>
<td>Measure the effect of having a calendar present in a patient’s room on Temporal Orientation Test Score.</td>
<td>Presence of calendar did not significantly affect TOT score (p=0.15).</td>
</tr>
<tr>
<td>Wilson et al., (2001;2005)</td>
<td>143</td>
<td>Patients randomized to receive intervention using pager or no treatment (control)</td>
<td>Patients using the pager achieved a greater number of target behaviours.</td>
</tr>
<tr>
<td>Bourgeois et al., 2007</td>
<td>38</td>
<td>Individuals were randomly assigned to either the Spaced Retrieval (SR) group or the didactic strategy instruction (SI) group.</td>
<td>Those in the SR group reported more treatment goal mastery than those in the SI group. Significant differences were not noted on the CIQ or the CDS post treatment in either group or between groups.</td>
</tr>
<tr>
<td>Boman et al., 2007</td>
<td>8</td>
<td>Subjects resided in specially equipped apartments (equipped with either basic or advanced EADLs) for 4 to 6 months</td>
<td>Subjects felt the EADLS were very useful and easy to learn. Occupational performance and quality of life was found to have improved.</td>
</tr>
<tr>
<td>Egan et al., (2005)</td>
<td>7</td>
<td>Patients received individual training on how to use the internet.</td>
<td>The majority of those participating reached moderate to high degrees of independence on using the internet.</td>
</tr>
<tr>
<td>Schmitter-Edgecombe et al., (1995)</td>
<td>8</td>
<td>4 subjects received 9 weeks of memory notebook training, 4 received 9 weeks of supportive therapy.</td>
<td>Notebook training group reported significantly fewer observed everyday memory failures (EMFs) than supportive therapy group at post-treatment (p&lt;0.05), but not at follow-up.</td>
</tr>
<tr>
<td>Burke et al., (2001)</td>
<td>5</td>
<td>Hospital staff prompting vs use of patient locator and reminder (PLAM) to direct patient to scheduled therapy sessions.</td>
<td>Using PLAM, need for human prompting reduced by 50%. Number of sessions requiring no prompting increased from 7 to 44%.</td>
</tr>
<tr>
<td>Hart et al., (2002)</td>
<td>20</td>
<td>Prospective, within-subject trial to test efficacy of portable voice organizer (Parrot Voice Mate III) to recall 3 therapy goals.</td>
<td>Recorded goals better recalled (p&lt;0.001) than unrecorded goals in both free (p&lt;0.005) and cued (p&lt;0.01) conditions.</td>
</tr>
<tr>
<td>Wilson et al., (1997)</td>
<td>15</td>
<td>ABA single case design measuring the effect of Neuro-Page (paging system) on individual memory targets.</td>
<td>Baseline: 37.08% mean success Treatment: 85.56% mean success Post-Treatment: 74.46% mean success.</td>
</tr>
<tr>
<td>Wright et al., (2001a)</td>
<td>12</td>
<td>Counter-balanced cross-over study of 2 computer organizers (HP 360LX &amp; Casio E10). Studied attitude, usage and correlation to psychometric tests.</td>
<td>No correlation between usage and psychometric tests. Results suggest conceptual understanding of electronic aid use a prerequisite to treatment benefit.</td>
</tr>
<tr>
<td>Wright et al., (2001b)</td>
<td>12</td>
<td>Exploring possible correlations between psychometric measures</td>
<td>No significant psychometric-usage correlations made. Familiarity with...</td>
</tr>
</tbody>
</table>

**Evidence-Based Review of Moderate to Severe Acquired Brain Injury**

http://www.abiebr.com

updated August 2013
### Table

<table>
<thead>
<tr>
<th>Authors</th>
<th>n</th>
<th>Intervention</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fish et al., (2007)</td>
<td>20</td>
<td>Looking at the impact of text messaging on prospective memory.</td>
<td>The cued messages individuals received lead to a higher degree of compliance with activities or goals to be completed.</td>
</tr>
<tr>
<td>van den Broek et al., (2000)</td>
<td>5</td>
<td>5 outpatients used the external aid, Voice Organizer, for a period of 3-weeks.</td>
<td>All patients benefited from the introduction of the voice organizer.</td>
</tr>
<tr>
<td>Manasse et al., (2005)</td>
<td>5</td>
<td>5 patients participated in two treatment programs: traditional and real-world treatment.</td>
<td>Gains made in the traditional setting were not consistently seen in the functional setting.</td>
</tr>
</tbody>
</table>

### Discussion

During the past year several studies were conducted looking at the effectiveness of various active reminders used to those with memory impairment.

In a study recently published RCT, Powell et al. (2012) compared trial and error learning to systematic instruction. Twenty-nine individuals were randomized to either the systematic instruction group (n=15) or the trial and error group (n=14). Twelve 45 minute training sessions were given to each individual. Each session targeted selected skills on a PDA. The systematic instruction condition emphasized mastery. Following treatment five areas were evaluated: post-test accuracy; maintenance accuracy; fluency; generalization; social validity. At the initial follow-up there were no significant differences between the groups, however, at the 30 day follow-up significantly differences began to immerge. Those in the systematic instruction group performed better at immediate posttest generalizing trained PDA skills when interacting with people, especially those other than the instructor. As well this group was found to be more fluent on task performance than those in the conventional instruction group (Powell et al., 2012).

McDonald et al. (2011) conducted an RCT cross over trial in which participants were randomly assigned to a Google calendar group, or a standard diary group. Prior to randomization, participants were asked to identify routines they would like to complete within the next 15 weeks. Following this individuals were randomized to either the Google calendar group (group A) or the standard diary group (group B). At the end of the 5 weeks, group A began using the standard diary and group B began using the Google calendar. Results indicate that memory aids helped to improve prospective memory performance of all participants. Google calendar was found to be more effective in improving prospective memory then the standard diary. Participants were
able to achieve 82% of their targets using Google calendar but only 55% of targets were achieved using the standard diary.

Lemoncello and colleagues (2011) randomly assigned 23 individuals into one of two groups. Those assigned to group A, the Television Assisted Prompting (TAP) group, had the TAP system installed on their television where they received reminders of events to be completed. Those in group B, the Assistive Technology for Cognition (ATC) group, received reminders through more traditional methods (paper planner, cell phones or computers). Following the 10 week intervention Group A received reminders in the more traditional way and group B began receiving reminders through the TAP system. The TAP system was found to improve task completion. This finding adds to the growing body of literature supporting the use of ATC to improve prospective memory post ABI.

In another RCT, 45 individuals were randomly assigned into one of 4 treatment groups (Shum et al., 2011). The treatment groups consisted of 4 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 completed it.

Dowds et al. (2011) recruited 36 adults to participate in a RCT using two different PDAs or a paper-based schedule book to assist them in remembering to complete various pre-selected tasks. Tasks completion rates were higher under the MOS and POS conditions. Participants using the POS PDA had a significantly higher task completion rate then those using the MOS PDA.

Wright et al. (2001a) examined the effect of two pocket computer systems containing three memory aides: appointment diary, notebook, and a to-do-list with a group of 12 ABI participants (9 TBI, 2 ABI). The type of pocket computer was counterbalanced and participants used each one for 8 weeks. No significant difference in use was found between type of pocket computer (they differed in terms of text entry – physical keyboard or touch-screen keyboard), and the majority (83%) used the three aids. Those participants who had previously used a memory aid made significantly more diary entries compared to those who had not previously used a memory aid. Severity of injury as well as level of cognitive function was not reported in this study. In another study by Wright et al. (2001b), findings were similar (i.e. no differences between computer
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Wilson et al. (1997) evaluated the efficacy of NeuroPage, a portable paging system, in reducing everyday memory problems in 15 ABI participants (10 TBI, 5 ABI). Using an A-B-A design, results indicated that all subjects significantly benefited from using the NeuroPage system and that following 12 weeks of use, performance remained at improved levels compared to baseline for another 3 weeks. Wilson et al. (2001) conducted a randomized controlled cross-over trial with 143 memory impaired patients, many – how many having sustained a TBI. The objective for this study was to evaluate a paging system designed to improve independence in people with memory problems as well as to reduce deficits in executive function. Results demonstrated that the pager system significantly increased patients’ ability to carry out daily tasks, and successful task achievement was more efficient after the pager intervention was introduced.

Hart et al. (2002) used hand-held recorders to remind moderate-to-severely impaired patients of their therapy goals (within subject design). Six individual goals were determined and half were recorded onto a hand-held organizer with an alarm preprogrammed to review the goals 3 times a day throughout the week. The other half of the goals were not recorded but were summarized at the weekly clinical management meetings. Goals were correctly recalled when using the hand held recorder compared to when goals were reviewed. It should be noted that the study examined only if the goals could be elicited during recall (either free recall or cued) and did not examine whether the subjects actually followed through with their goals.

Burke et al. (2001) used a complex computerized tracking system (patient locator and reminder system – PLAM) to remind and direct 5 patients on an acute rehabilitation unit to their next therapy appointment. The electronic tracking system prompted patients 10 minutes in advance of their appointments and continued to do so until the patient started moving toward the therapy room. If patients were going in the wrong direction, the system would prompt them on how to get to the appointment and would offer positive reinforcement as the patient made their way to the therapy room. Using a case series design, baseline data was gathered for a week and included the number of staff prompts needed to get the person to scheduled therapy and the time the person arrived at the therapy. Once the patients were introduced to the PLAM system, data was collected for a 3-day period. Results indicated that the subjects arrived earlier to their appointments and required fewer prompts (i.e. the number of sessions that did not require prompting increased from 7% to 44%).

In a prospective controlled study completed by Bourgeois et al. (2007), 38 subjects, along with one significant other for each subject, were assigned to either the spaced retrieval (SR) group or the Didactic strategy instruction (SI) group. Subjects were asked systems in terms of use of memory aids).
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To maintain a daily log where they would note all areas they were having difficulties in. Treatment goals were developed based on areas of difficulty. Those in the SR group were given prompt questions and responses for each goal selected. Answers to the prompt questions were expected to be given in exactly the same way each time. Those in the SI group received time with a therapist to discuss memory strategies. All sessions were conducted by phone for both groups. Results indicate that the frequency of memory problems decreased in both groups over time. Significant improvement in goal mastery (p<0.05) was noted in the SR group but not in the SI group. Scores on the Cognitive Difficulties Questionnaire (CDS) indicate both groups were experiencing fewer difficulties following treatment. Post treatment, scores on the community integration questionnaire (CIQ), showed no significant differences between the two groups.

Boman et al. (2007) invited 8 participants live in one of two apartments equipped with electronic aids to daily living (EADLs). Participants, one in the apartment, were given 4 or 5 sessions weekly, each lasting 1 to 2 hours on how use the EADLs. Init would do; however, post study results indicate improvement in the self-perceived ability to perform important activities and in the satisfaction with performing tasks (p<0.05). For 6 participants improvement was also seen on the Sickness Impact Profile (SIP) 136. Study results indicate occupational health and quality of life had improved. Overall the authors found that EADLs may play a role in facilitating everyday functions.

In a study conducted by Egan et al. (2005) individuals who had sustained a TBI were instructed on how to use the internet. Each participant was given one-on-one instruction in their own home. Following training, individuals showed significant improvement on their level of independence in using the internet (p<0.028). Less improvement was noted when looking at the tasks that required greater abstract understanding and required more steps to complete. Participants’ were able to complete concrete tasks using fewer steps with greater ease.

Using a memory notebook as the external memory aid, Schmitter-Edgecombe et al. (1995) assigned 8 individuals with severe closed-head-injury and memory deficits into either a notebook-training group or an interpersonal support group (control). Groups were matched on a number of demographic variables. Outcome measures included both performance on memory tests as well as observation and responses to a questionnaire on everyday memory failures. Both groups received 2, 1-hour sessions per week for 8 weeks (16 sessions). Results indicated that, on cognitive measures of memory functioning, there was no difference between groups. However, on observed everyday memory failures (questionnaire), performance improved (i.e., less failures) following treatment, although performance was not maintained at 6-month follow-up.

In a randomized controlled trial, Watanabe et al. (1998) examined whether use of a
calendar would enhance orientation following an acquired brain injury. Results indicated that the presence of a calendar did not enhance performance on a temporal orientation test (date and time). It is difficult to judge the outcome of this study as no scores were reported for either the control or treatment group, and it is not clear whether post-traumatic amnesia, and/or severity of injury had an impact on performance.

Ownsworth and McFarland (1999) evaluated two different training approaches in the use a diary to compensate for memory problems. They randomly assigned 20 ABI volunteers (15 TBI; 5 ABI) to either a Self-Instructional Training (SIT) approach or to a task-specific learning approach. The Diary-SIT approach trains compensation using higher cognitive skills of self-regulation and self-awareness. That is, participants where taught to question themselves with the following script (WSCT): What are you going to do? Select strategies; Try it out; Check how it’s working. By using this training approach, the researchers speculated that it provides direct, internal feedback, which can generalize to other situations involving memory. In contrast the Diary-Only approach taught subjects how to use the diary. Results indicated that those in the Diary-SIT group made consistently more diary entries, reported a reduction in everyday memory problems and made more positive ratings on treatment efficacy compared to the Diary-Only group.

In a study conducted by Fish et al. (2007), all participants (n=20) were given cell phones and asked to make calls a specific times of the day. To aid them in remembering, participants were sent text messages. Results indicate that the texting a reminder to participants resulted in significantly more calls (p<0.001) being made then when they were not sent a message.

Van den Broek et al. (2000) evaluated the effectiveness of the compensatory external aid, the Voice Organizer for five individuals following brain injury. All five participants benefited from the use of the Voice Organizer as measured by the Message-Passing Test. For four of five patients, there was no significant improvement or deterioration in positive or negative affect during the course of the study.

In a case series, Manasse et al. (2005) exposed subjects to 2 treatment measures to aid them in memory recall. The traditional treatment was designed to assist subjects with memory recall, by pairing pictures of staff with an imagery statement, while the real-world treatment consisted of name restating, phonemic cueing and visual imagery to assist subjects in remembering names. Results from the traditional treatment indicated 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. During the cueing condition of the real world treatment sessions only 2 names were consistently used by each subject. The
visual memory program was the only program where subjects consistently used both target names. When questioned directly 4 of the 5 subjects could consistently identify one or both of the target names. Because subjects did not use the names was not indicative of whether or not they knew them.

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.”

Conclusions

There is Level 1a evidence supporting the use of active or high tech external aids (assistive technology) as a compensatory strategy for memory impairments.

There is Level 2 evidence supporting the use of passive or no tech/low tech aids in improving memory impairments post ABI.

External memory aids have been shown to be an effective compensatory strategy for memory impairments.

6.2.1.2 Computer-Assisted Training

A specific intervention for improving general cognitive functioning is computer-assisted training. The use of computer-assisted cognitive retraining has multiple potential benefits within the rehabilitation setting following brain injury. Computer retraining allows for flexibility in retraining procedures, increased individuality of therapy programs and also decreases the amount of direct time a therapist is with the patient. It also has the potential of continuing cognitive retraining within the community setting. Furthermore, as presented at the NIH Consensus Development Panel (1999) computer-assisted strategies are used to improve neuropsychological processes, including attention, memory and executive skills.

In recent years, clinicians have recommended the use of computers as an efficacious tool in cognitive rehabilitation. One study investigated the efficacy of computer-assisted rehabilitation in comparison to non-computerized methods (Tam and Man 2004). Eight studies were identified that used computer-assisted measures for cognitive rehabilitation following brain injury.
### Individual Studies

#### Table 6.8 The Use of Computer Assisted Training to Enhance Executive Function

<table>
<thead>
<tr>
<th>Author/Year/Country/Study design/PEDro Score</th>
<th>Methods</th>
<th>Outcome</th>
</tr>
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<tbody>
<tr>
<td>Dou et al., (2006) Hong Kong, (China) RCT PEDro = 5</td>
<td><strong>N=37</strong> Participants were randomized to 2 memory training programs: the computer assisted memory training group (CAMG) and the therapist administered memory training group (TAMG). Each group received 1 month memory training programs that were similar in content but delivered differently. The control group received no training. Those in the treatment groups received 20 training sessions. Sessions ran for 6 days each week and lasted approx 45 mins. Post treatment follow up lasted for one month. Sessions consisted of training a basic component memory skills, in the management of typical daily tasks utilizing/integrating the component memory skills, in customized programs and skill consolidation as well as in the generalization of those skills in practice.</td>
<td>Scores from the NCSE indicate that there was a significant increase in the TAMG (p&lt;0.015) and the CAMG (p&lt;0.02) on the memory sub-test of each scale compared to the control group. When looking at the results of the scores on the RBMT test, there was only a significant difference between the CAMG and the control group (p=0.0001).</td>
</tr>
<tr>
<td>Bergquist et al., (2009) USA Non-RCT</td>
<td><strong>N=14</strong> Participants were placed in one of two intervention groups: an active calendar acquisition intervention group or the control diary intervention group. Throughout each intervention participants had 30 sessions with a therapist and sessions were completed via the internet using instant messaging. Participants were placed in one of the 2 groups and at the end of the 30 sessions they began “other” condition. During the calendar condition, participants were encouraged to use the on-line calendar to plan events and to remind them of these events. During the diary condition, participants were asked to use their diary to keep track of their day to day events and occurrences. The IM sessions were used to review what (work, appointments) was completed during both types of sessions.</td>
<td>There were no significant difference between the two sessions on memory functioning as noted on the neurobehavioral functioning inventory (NFI) (p&gt;0.05). From time 1 to time 2, improvement was found on the compensation techniques questionnaire (CTQ): specifically the notes on calendar (p&lt;0.02) and the use of cue cards (p&lt;0.01). Family members also noted improvement in levels of depression (p&lt;0.02) from time 1 to time 2. Family also felt the patient’s memories had improved.</td>
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<tr>
<td>Author/Year/Country/Study design/PEDro Score</td>
<td>Methods</td>
<td>Outcome</td>
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<tr>
<td>Tam and Man (2004) China Non-RCT</td>
<td>N=34 A study of adults with post-head injury amnesia due to closed-head injury was conducted to assess the effectiveness of computer-assisted memory retraining programs. Participants were randomly assigned to one of four treatment groups (matched diagnostically and demographically): (1) self-paced group; (2) feedback group; (3) personalized group; and (4) the visual presentation group. Each group went through one of the four computer-assisted memory re-training strategies. Each participant was involved in 10 sessions, approximately 20-30 minutes in length. The Rivermead Behavioural Memory Test (RBMT) was used to evaluate self-efficacy.</td>
<td>After intervention, in any one of the four computer-assisted memory programmes, patients performed significantly better in memorizing and remembering ‘drilled content’ (p&lt;0.05). All four 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.</td>
</tr>
<tr>
<td>Chen et al., (1997) USA Case-Control</td>
<td>N=40 Closed-head TBI subjects matched for diagnosis, age &gt;= 18 years, education ≥ 9 years, chronicity, severity and time between testing were divided retrospectively into computer-assisted rehabilitation (CACR) and tradition therapy groups. Pre and post-treatment scores of neuropsychological tests; attention, visual-spatial ability, memory and problem solving ability measured by the WAIS-R, and WMS.</td>
<td>Experimental group showed significant improvement (all values p&lt;0.004 with Bonferoni Connection): category test – trails A &amp; B, WCST, logical memory delayed, visual reproduction immediate, VIQ, PIQ, FSIQ, information, digit span, vocabulary, PC, OA, DSYM. Comparison group made significant gains in trails B, PIQ, FSIQ, picture arrangement, block design, OA and DSYM.</td>
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<tr>
<td>Gentry et al., (2008) Canada Pre-Post</td>
<td>N=23 individuals at least one year post injury participated in the following study. Participants were each given a PDA and trained in how to use by an occupational therapist (OT).</td>
<td>Pre and post test assessments indicate significant improvements in satisfaction with performing everyday tasks following PDA training. Improvements were noted when looking at post training performance and post training satisfaction (p&lt;0.001). Scores on the CHART-R self-assessment rating scale showed improvement as well. Significant improvement was seen on the scores of the cognitive independence, mobility, and occupation subsections of the test (p&lt;0.001)</td>
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</table>
| Sohlberg et al., (2003a) USA                 | N=8 A pilot study of subjects with acquired cognitive-linguistic impairments receiving electronic mail | Types of errors observed in composing emails that were not related to the mechanics of the
### Author/Year/Country/Study design/PEDro Score

<table>
<thead>
<tr>
<th>Methods</th>
<th>Outcome</th>
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<tbody>
<tr>
<td>Intervention. An analysis for errors and subject preference was assessed.</td>
<td>Email or word-processing was variable across all participants in all conditions. There was considerable variation in patient preference.</td>
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</table>


**USA**

**Case Series**

**N=12** Subjects (11 TBI and one CVA) were introduced to a supervised usage trial of a palmtop computer that included scheduling software capable of generating audible reminder cues. Nine subjects (75%) reported that the palmtop computer had been a useful tool. Seven of these 9 patients expressed that they continued to use the computer following the completion of the study. All patients recommended that the computer continue to be used in outpatient brain injury rehabilitation.

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

### Discussion

In a RCT conducted by Dou et al. (2006), participants were randomized to one of two groups: the computer assisted memory training group (CAMG-treatment - group 1) or the therapist administered memory training group (TAMG-treatment - group 2) with each receiving one month memory training. Memory training was similar between the groups but they were delivered differently. The treatment groups received 20 training sessions with each running for 6 days per week and lasting approximately 45 minutes. The control group received no training. Sessions consisted of: training basic component memory skills in (1) the management of typical daily tasks utilizing/integrating the component memory skills, (2) customized programs and (3) skill consolidation as well as in the generalization of those skills in practice. Scores on the neurobehavioural cognitive status examination (NCSE) showed significant improvement in the TAMG and CAMG groups (p<0.015, p<0.02 respectively) compared to the control group. Results from the Rivermead Behavioural Memory Test (Cantonese version) showed the CAMG improved significantly compared to the control group (p<0.0001).Those in the TAMG showed no significant improvement.

Self-practice, presentation of attractive stimuli, multi-sensory feedbacks and personalized training contents were the four different forms of computer-assisted cognitive re-training programmes that Tam and Man (2004) used to evaluate people with post-head injury amnesia. Participants were randomly assigned to one of four treatment groups (matched diagnostically and demographically): (1) self-paced group, which allowed individuals to move at their own pace in a non-threatening environment; (2) feedback group, which involved immediate provision of feedback in a non-judgmental fashion; (3) personalized group, whereby the computer presented training...
contents showing the participant’s actual living environment and routines; and (4) the visual presentation group, which was a provision of attractive and bright presentation designed to help individuals engage in the activity. Each group went through one of the four computer-assisted memory re-training strategies. Results revealed that the patients in the experimental group showed positive improvements on all of the four memory training methods as compared to the control group. However, there were no statistically significant differences among the four training methods. Nonetheless, this study showed that computer-assisted memory retraining yield positive results for patients with memory post-head injury amnesia. Similarly, in a non-controlled study by Kim et al. (2000), all 12 patients that took part in a trial investigating the efficacy of a palmtop computer for use in daily activities, recommended that this treatment continue to be used in outpatient brain injury rehabilitation.

Chen et al. (1997) studied the effect of computer assisted cognitive rehabilitation versus traditional therapy methods. Within-group comparisons of pre- and post-intervention measures demonstrated significant gains on multiple psychometric tests taking into account multiple statistical comparisons. However, multivariate analysis comparing the experimental and control groups across the domains of attention, visual-spatial, memory and problem solving did not demonstrate significant differences between the groups.

In a recent study conducted by Bergquist et al. (2009), individuals were asked to participate in either an active calendar acquisition intervention or a control diary intervention program. Participants were assigned to one of the two interventions and once completed they began the second intervention. Sessions were completed on line using an instant messaging system. Improvement was noted in calendar use and using a cue card (p=0.02, p=0.01 respectively). Family members noted an improvement in mood and memory problems post intervention.

Gentry et al. (2008) conducted pre and posttest assessment on a group of 23 individuals with a TBI living in the community. Due to problems with memory, all participants were found to have difficulties with everyday tasks. To assist them in improving their memory a PDA was given to each individual and training was provided by an occupational therapist. Following training, participants reported improved in satisfaction with performing everyday tasks. Improvements were noted when looking at post training performance and post training satisfaction (p<0.001) and on the scores on the CHART-R self-assessment rating scale. Overall significant improvement was seen on the scores of the occupation, cognitive independence, and mobility subsections of the test (p<0.001).

Electronic mail (email) may prove useful for reducing the experience of social isolation for patients sustaining acquired cognitive-linguistic impairments (Sohlberg et al., 2003).
The authors were interested in the usability and patient preference of a simplified email interface on eight brain injured patients. Patients were asked to read and reply to four prompt conditions: no prompt, idea prompt, fill-in-the-blank prompt and multiple-choice prompt. Difficulties encountered included computer usability and message composition. Results identified three categories of usability problems: lack of knowledge concerning functionality of keys for word-processing operations, poor conceptual understanding for the mouse operation and poor use of interface prompts. Results also found that there was considerable variation among patient preferences and the types of errors observed in composing emails, and that all patients legitimized the use of email interfaces as a means of reducing social isolation.

**Conclusions**

There is conflicting evidence supporting the use of computer assisted cognitive retraining as an adjunct to the rehabilitation program, especially regarding attentional retraining following brain injury. Although some improvement in memory was found in a few of the studies it was not found in all. General cognitive functioning did appear to benefit from computer assisted cognitive retraining; however, further study confirming these findings need to be conducted.

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Computer-assisted training has been shown to have a positive effect on general cognitive functioning, but has not yet been shown to be an effective treatment for the remediation of memory and attentional deficits.

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6.2.1.3 Virtual Reality and Cognitive Functioning

One study was identified that used an innovative approach to improving cognitive function following brain injury, using a non-immersive, virtual reality component to promote exercise and cognitive functioning.

**Individual Studies**

**Table 6.9 Virtual Reality (VR) Exercises and Their Impact on Cognitive Functioning**

<table>
<thead>
<tr>
<th>Author/Year/Country/Study design</th>
<th>Methods</th>
<th>Outcome</th>
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<tbody>
<tr>
<td>Grealy et al., (1999) Scotland</td>
<td>N=13 Ambulatory TBI subjects with no perceptual disabilities participated in a random allocation crossover study that</td>
<td>Intervention group (n=13) performed significantly better than control group (n=320) on digit symbol (p&lt;0.01), verbal</td>
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</table>

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http://www.abiebr.com  
updated August 2013
Non-RCT | used non-immersive virtual reality exercises to test attention, information processing, learning, memory, reaction and movement times. Information for 320 patients was collected and acted as the control for this study. 
---|---

Zhang et al., (2001) USA Case Control | N=60 VR kitchen was designed to test the skills of those who had sustained a TBI. Participants are outfitted with a VR head set, personal computer platform with a sound card, head mounted 3-dimensional glasses. To assist in completing the task the software allowed for cues and prompts in response to the user’s sequence of actions or lack of. Participants are given a task to complete. All participants performed the task 2 in 10 days. Assessment of participants revealed the non-TBI participants performed better then those with a TBI during both test phases. Those with a TBI had difficulty processing the information presented to them, completing the assessment and working through the task in a logical way. Speed at which the task was completed from time 1 to time 2 did not significantly improve for the TBI participants, it did improve for the non-TBI participants.

**Discussion**

Grealy et al. (1999) addressed the effects of exercise and virtual reality post brain injury. This study evaluated the impact of an exercise program, which used a stationary bicycle in conjunction with non-immersive virtual reality administered over a minimum of 4 weeks. The results demonstrated significant benefits in the experimental group pre and post intervention for learning and memory tasks. Similarly, when compared to historical controls, the experimental group fared significantly better on digit symbol as well as visual and verbal learning tasks.

In a study by Zhang et al. (2001) 60 individuals (30 of them had suffered a TBI) participated in a study which tested their skills in a virtual reality kitchen. Participants were given a task to complete (twice in ten days) and were given cues to assist in completing the task. Individuals who had sustained a TBI did not perform as well as those without a TBI. Individuals with a TBI were slower, experienced difficulty in processing information presented to them and were unable to work through the task in a logical way.

**Conclusions**

*There is Level 2 evidence of a positive impact on visual and verbal learning post exercise intervention for brain injury survivors.*

*There is Level 3 evidence from one study indicating that VR programs do not enhance cognitive functioning post TBI in individuals who have sustained a TBI.*
Virtual reality programs may enhance the recovery of visual and verbal learning following brain injury; however more study needs to be completed as currently there is limited evidence supporting the use of VR programs.

6.2.2 Internal Aids
The following studies examined how internal aids could be used to enhance memory following an ABI.

Individual Studies

Table 6.10 The Use of Internal Aids to Enhance Memory Post ABI

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<thead>
<tr>
<th>Author/Year/Country/Study Design/ PEDro Score</th>
<th>Methods</th>
<th>Outcome</th>
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<tr>
<td>Potvin et al., (2011) Canada Non-RCT</td>
<td>N=30 Individuals were assigned to either the experimental group (n=10) or the control group (n=20). Those assigned to the experimental group participating in a 10 prospective memory rehabilitation groups lasting 90 minutes. The Test Ecologique de Memoire Prospective (TEMP) was used to evaluate change in the experimental group.</td>
<td>The experimental group performed significantly better on the TEMP post PM training (p&lt;0.05) than the control group. During the learning phase cued recall improved for those in the experimental group, although this improvement was not found to be significant. Participants who took part in the rehabilitation program improved their performance on the PM experimental task. These changes were seen when performing everyday tasks.</td>
</tr>
<tr>
<td>Twum and Parente (1994) USA RCT PEDro = 3</td>
<td>N=60 Consecutively referred TBI subjects from Maryland State Dept. of Vocational Rehabilitation (mean age: 21 years) were randomized into four groups: no imagery / verbal labeling; imagery / no verbal labeling; imagery / verbal labeling and a no imagery / no verbal labeling (control). Delayed recall and trials to criterion were measured on the VerPA and VisPA tasks.</td>
<td>MANOVA analysis revealed an overall significant main effect of mental imagery instructions (p &lt; 0.0001) and a main effect of verbal labeling instructions on the VisPA (p &lt; 0.0001).</td>
</tr>
<tr>
<td>Milders et al., (1995) Netherlands Follow-up to Berg et al. (1991)</td>
<td>31 of 39 subjects participated in a four year follow up of the Berg et al. (1991) RCT that compared Memory Strategy training vs. Drill and Practice vs. no treatment. Follow-up consisted of control</td>
<td>Standardized memory sum scores at long-term are significantly lower in the three patient groups than in the normal control group (p&lt;0.05). Drop out effect on follow-up results was significant (p&lt;0.05). The</td>
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<tr>
<td>Author/Year/Country/Study design/ PEDro Score</td>
<td>Methods</td>
<td>Outcome</td>
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<tr>
<td>Tailby &amp; Haslam (2003) Australia Non-RCT</td>
<td>N=24 TBI subjects with acquired deficits in explicit memory were divided into groups of 8 based on Verbal Memory Index (VMI) score, and matched across groups in terms of age, gender, premorbid and current intellectual functioning. Ninety-six 5-6 letter concrete nouns were used over two sessions to practice 3 learning conditions: errorful, errorless (examiner generated), and errorless (self-generated). Following the learning tasks, memory was tested explicitly and implicitly 5 and 30 minutes after study phase generating 6 scores for each learning condition at both testing times.</td>
<td>Cued recall performance following self-generated errorless learning was significantly better than standard errorless learning conditions (p&lt;0.0001). Level of priming did not differ significantly between groups (p&gt;0.05). Memory performance was significantly better following errorless learning (examiner generated) activity (p&lt;0.0001). Mild and moderate groups performed significantly better than severe group (defined by VMI – p&lt;0.0001)</td>
</tr>
<tr>
<td>Evans et al., (2000) Non-RCT</td>
<td>A three-phase consisting of 9 experiments was conducted to compare the effects of two internal, memory techniques: errorless learning and trial-and-error learning in both short and long delay recall conditions. Brain-injured patients were trained to use these techniques and comparisons were made (phase 1 n=18; phase 2 n=16; phase 3 n=34)</td>
<td>It was demonstrated that the more severely memory-impaired patients benefitted to a greater extent from errorless learning than those with less severe conditions. It should be noted that this benefit may not apply when the interval between learning and recall is relatively short.</td>
</tr>
<tr>
<td>Goldstein et al., (1996) USA Non-RCT</td>
<td>N=30 subjects with ABI who had sustained a serious closed head injury within 1 year of assessment and suffered a significant impairment of memory but with an absence of generalized dementia received computer training programs with (self-directed help software) and without (human trainer) assistance. Tasks focused on word lists (15 sessions, 2-3 times per week) and face association (10 sessions). The data for the “without” group derived from a 1988 study by same author.</td>
<td>Both original (p&lt;0.01) and computer-assisted (p&lt;0.001) methods were significant in word list tasks. Delayed recall of face/name tasks was found to be significant in computer assisted trials (p&lt;0.01). The number of trials to learn lists was significant in original (p&lt;0.01) and computer assisted (p&lt;0.05).</td>
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<tr>
<td>Author/Year/ Country/Study design/ PEDro Score</td>
<td>Methods</td>
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<tr>
<td>Constantinidou &amp; Neils (1995) USA Case-Control</td>
<td>N=40 Study compared performance on a recall task for ABI cases (n=24), compared with healthy controls (n=16). Word lists presented under three conditions: auditory, visual, and auditory plus visual.</td>
<td>Results indicate that the auditory condition was the least effective for learning compared with both visual and auditory-visual (p=0.003). There was no significant difference between visual and auditory-visual conditions (p=0.091).</td>
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<tr>
<td>Glisky &amp; Delaney (1996) USA Case-Control</td>
<td>N=16 TBI patients (mean LOC 10 days) who experienced PTA (mean of 53 days) participated in 3 separate sessions practicing stem completion of 4-7 letter words using cued recall, free recall and recognition.</td>
<td>Priming effect in PTA patients was not significant from the controls (p&gt;0.05), but was significant within the PTA group (p&lt;0.05) – compared to those without prior exposure to word lists. Controls substantially improved their results when given explicit instructions while PTA patients performed equivalently. Control group recalled significantly more words than the PTA group (p&lt;0.01). None of the PTA patients were able to recall any of the list items, made significantly more false alarms (p&lt;0.01).</td>
</tr>
<tr>
<td>Milders et al., (1998) Netherlands Case-Control</td>
<td>N=26 13 closed-head injury subjects (mean PTA 36 days) and 13 healthy controls matched on age and level of education participated in 8 individual 60-90 minute sessions over four months using exercises with standardized instructions that help make the new name more significant to the learner.</td>
<td>ANOVA (cases vs controls, baseline vs post-training were significant for group (p&lt;0.01), evaluation moment (p&lt;0.001), and interaction (p&lt;0.001). At follow up, only verbal learning scores reached significance (p&lt;0.01).</td>
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<tr>
<td>Ewert et al., (1989) USA Case-Control</td>
<td>N=32 A series of memory tests (procedural and declarative) were administered to 16 subjects with severe closed head injuries (GCS &lt;= 8) and 16 neurologically intact control subjects. Results were compared between groups.</td>
<td>Mirror Reading (p&lt;0.001), Porteus Maze (no values provided), Pursuit Rotor (both tumble speeds - p&lt;0.001), and Declarative Memory (p&lt;0.001) tests significantly improved once PTA phase had resolved.</td>
</tr>
<tr>
<td>Author/Year/Country/Study design/ PEDro Score</td>
<td>Methods</td>
<td>Outcome</td>
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<td>---------------------------------------------</td>
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<tr>
<td>Thoene and Glisky (1995) USA and Germany Pre-Post</td>
<td><strong>N=12</strong> TBI Subjects in a comparative, multiple intervention study in the USA and Germany. Interventions focused on learning name – face associations using a mnemonic training technique combining verbal elaboration and visual imagery, a vanishing cues method, and a video presentation. Success was measured by the number of correct name-face associations and trials necessary to achieve criterion.</td>
<td>The number of correct name/face associations required to achieve criterion decreased significantly ($p = 0.001$). Patients needed significantly fewer trials to reach criterion in the mnemonic condition than the other conditions. The number of cues needed to produce the names during training decreased rapidly across the first few sessions, then tended to asymptote at approximately one cue per name.</td>
</tr>
</tbody>
</table>

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

**Discussion**

In a recent study Potvin et al. (2011) assigned 30 moderate to severe TBI patients to either an experimental group (n=10) or a control group (n=20). Both groups were matched based on age and education. All participants were initially assessed using the TEMP. Those in the experimental group participated in ten prospective memory training sessions. Each session lasted 90 minutes. The PM program was divided into 5 phases: understanding PM functioning; training to visualize simple images; learning visual imagery techniques; applying visual imagery in PM; and applying visual imagery in everyday situation. The scores on the TEMP, following treatment, improved for those in the experimental group. Study authors also noted that those in the experimental group reported fewer symptoms of depression than the control group.

Twum and Parente (1994) randomly assigned 60 TBI patients into one of 4 groups (one control and three mnemonic strategy groups) counterbalanced. The researches demonstrated improved performance for subjects who were taught a strategy (either verbal labeling or visual imagery) while learning paired-associations. Treatment groups showed greater efficiency in learning and greater delayed recall information.

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.

Goldstein et al. (1996) evaluated a visual-imagery technique (“Ridiculously Imaged Story” technique (RIS)) in training severely brain injured individuals to learn and recall lengthy word lists. Participants were asked to read a story where 20 words are presented in
bold-face and subjects were instructed to remember the bold-face words for later recall. If subjects could not recall all the words they were provided with (1) the part of the story in which the word appeared and if that didn’t aid recall, they were then provided with (2) a category cue for the word. It should be noted that in both studies reviewed, a number of their subject pool (N=10) came from a previous study (Goldstein et al., 1988). Goldstein et al. (1996) evaluated whether there were differences between a computerized and non-computerized version of RIS and another visual imagery technique (Pictorial Imagery). Results indicated that although the computerized versions resulted in a slightly better performance on learning trials, the difference was non-significant.

By using the various visual imagery techniques to aid learning and recall, researchers have demonstrated that increasing the saliency of features encoded, results in an increase in the amount recalled. 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 etc). When subjects (13 severely TBI vs. 13 matched controls) were tested on 3 different memory tasks, results indicated a significant difference following training, more so for the control group than the TBI group. 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).

In a 4 year follow up study, to one conducted by Berg and colleagues, Milder et al. (1995) found the effects at 4 months were no longer evident at 4 years (all groups were equivalent). In the original study, Berg et al. (1991) demonstrated that severely brain injured patients demonstrated improved effects on objective measures of memory at 4 months following training in a strategy-use group compared to a pseudo-treatment and a no treatment control group. In the strategy group, individuals were taught general cognitive principles of memory functioning and aids (i.e., internal and external strategies were taught and practiced). In contrast, the pseudo-treatment group practiced memory games and tasks with no explanation.

How individuals learn (i.e., encode) information will determine to a large extent what is later recalled. Twum and Parente (1994) demonstrated that if an active strategy (either verbal labeling for visual information or visual imagery for verbal information) is taught to individuals while learning the paired associations, learning and recall is enhanced (i.e., fewer trials needed to reach criterion during learning and improved recall following a delay). Tailby and Haslam (2003) also examined how learning can improve or limit later recall of information. They had 24 ABI subjects matched on basis of age, gender, premorbid and current intellectual status divided into 3 groups based on performance.
of verbal memory (mild, moderate & severe). Each group (n=8) was randomly assigned to one of 3 learning conditions: errorless learning, self-generated; errorless learning, experimenter generated; and errorful learning. Results showed that regardless of severity level, subject recalled more information in the errorless learning conditions (with self-generated superior to experimenter generated) than in the errorful learning condition.

Constantinidou and Neils (1995) examined the effects of stimulus modality on verbal learning of patients with moderate-to-severe closed head injury and a matched control group. Results indicated that when information is presented visually (with and/or without auditory presentation of names) more information is learned than when information is presented within the auditory modality alone. As expected, patients learn new information at a significantly slower rate compared to controls.

It is generally thought that while patients are experiencing post-traumatic amnesia (PTA), they are not able to learn and retain new information, and as a result, cognitive rehabilitation is usually postponed until PTA has resolved. This tends to be true if using tasks of explicit or declarative learning and recall. Two studies were reviewed that reported that PTA patients were capable of learning and retaining new information when task demands were dependent on implicit/procedural learning. Glisky and Delaney (1996) evaluated implicit memory (priming using a stem completion task) and the use of vanishing cues when learning semantic information in a small number of TBI patients (n=8 & 4) who were still experiencing PTA and a matched control group. Findings revealed that learning and recall of information (once PTA has resolved) had occurred, albeit at reduced levels compared to controls. Ewert et al. (1989) also demonstrated procedural learning and retention in a group of 16 severely closed head injured participants and matched controls.

Conclusions

There is Level 2 evidence (from several studies) that internal strategies appear to be an effective aid in improving recall performance.

Internal strategies appear to be an effective aid in improving recall performance.

6.2.3 Memory Programs

Following an ABI or TBI one of the most persistent problems are memory deficits. 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., 2010). Internal memory strategies have also met with limited success.

**Individual Studies**

### Table 6.11 Use of Memory Retraining Programs to Enhance Memory

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<tr>
<th>Author/Year/Country/Study design/PEDro Score</th>
<th>Methods</th>
<th>Outcome</th>
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<tbody>
<tr>
<td>Thickpenny-Davis &amp; Barker-Collo (2007) RCT New Zealand PEDro = 5</td>
<td>N=14 Individuals were randomly assigned to either the treatment group (memory rehab group) or the waitlist control group. Those assigned to the treatment group participated in a memory rehabilitation program. The memory group consisted of 8 learning modules, each 1 hr in length and held 2x a week for 4 weeks. Didactic teaching about memory and memory strategies, small group activities, discussions, problem solving, practice implementing memory strategies was used. Errorless learning was also used when reviewing materials.</td>
<td>Overall improvement was seen for the treatment group across the various time periods. When comparing pre-group results on the various memory scales, improvement was seen at time of post group testing and again at follow-up.</td>
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<tr>
<td>O'Neil-Pirozzi et al., (2010) USA Non-RCT</td>
<td>N=98 Individuals were assigned to either the experimental group (n=57) or the control (wait-list group n=41).12-90 minute sessions, held 2 x weekly for 6 weeks intervention sessions were held. The intervention included memory education and emphasized internal strategy acquisition to improve memory function from encoding, storage and retrieval perspectives. Primary emphasis was placed on semantic association (categorization and clustering), followed by semantic elaboration/chaining and imagery.</td>
<td>Pretesting revealed a significant difference between both groups on the Hopkins verbal learning test-revised (HVLT-R) only. Individuals who had had a severe TBI performed more poorly on the HVLT-R than those with moderate injuries. 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 from week 1 to week 7. Results of the Rivermead Behavioural Memory test II revealed similar results. Overall memory performance was improved for all those in the experimental group compared to the control group.</td>
</tr>
<tr>
<td>Scheff et al., (2008) USA Non-RCT</td>
<td>N=20 The authors report on 2 studies they conducted with individuals who had sustained a mild, moderate or severe BI.</td>
<td>Study 1: self-generation encoding procedures improved recognition memory test performance, but not free recall, compared with the didactic</td>
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</table>
### Methods

**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 pairs were presented in the same order at testing as they had been presented during the learning trials.

**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.

### Outcome

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<th>Author/Year/Country/Study design/PEDro Score</th>
<th>Methods</th>
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<tr>
<td><strong>Study 1:</strong> N=28 Both individuals who had sustained a TBI and those who had not were enrolled in this study. Each group was presented with 48 verbal paired associated. These were divided across 3 learning conditions (massed restudy, spaced restudy and retrieval practice). During the <strong>massed restudy</strong>, paired words were presented for 6 s followed by 2 6s restudy trails. During <strong>spaced restudy</strong>, participants were shown paired words for 6 s. followed by presentation. Study 2: self generation strategy improved cued recall but not free recall compared with the didactic condition. 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.</td>
<td><strong>Study 2:</strong> The effects of the various learning strategies were tested with a delayed cued recall task after 45 min of unrelated cognitive tasks. Retrieval practice was found to result in the best recall. This was followed by spaced restudy, and finally massed restudy. Those with a TBI performed worse than those with out a TBI. For those</td>
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</table>
### Author/Year/Country/Study design/PEDro Score

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<th>Methods</th>
<th>Outcome</th>
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<tr>
<td>3 filler trails each 6 s and a 6 s restudy trails, six filler trails (6s) and another 6s restudy trail. During the <strong>retrieval practice</strong>, paired associates were presented for 6s followed 3 filler trials and a re-exposure trail consisting of 5 s cued recall test and a 1 s feedback screen.</td>
<td>with a TBI, retrieval practice was the best learning strategy.</td>
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USA  
Case Series  

**N=20** 80 words were selected, (low-medium frequency words-6-11 letters long; printed in upper case on index cards). Once group of words was presented once; another group of words was not presented but appeared on the recognition sheet. There were 4 groups of 20 words, 4 separate words lists (once-presented, massed and spaced). Participants in groups of 5 were randomly assigned to each of the 4 study lists constructed for counter-balancing purposes. They were asked to ready the work and rank it from 1 to 10 on how familiar they were with it. The learning of the word list was assessed by asking patients to recall the list immediately after its presentation and then 30 minutes later with a free recall and recognition test after a 30 min delay.  

Spaces words were more likely to be recalled during the immediate recall than massed words (p=.018). On the delayed recall spaced words were more likely to be correctly recalled than massed words or once presented words during delayed recall performance. On the recognition performance test, individuals were able to correctly identify spaced words over massed or once presented words. Over all individuals with a moderate to severe TBI can improve their memory by altering the manner in which learning takes place.  

Quemada et al., (2003)  
Spain  
Pre-Post  

**N=12** Severe TBI subjects (GCS mean 5.7, PTA > 28 days) with a memory impairment that interfered with autonomy in ADL, and scored below the 10th percentile on both the CVLT and REY, received individualized treatment using Wilson’s Structured Behavioral Memory Program in 50 minute sessions daily for 6 months. REY, CVLT, RBMT, MFE tests were measured at baseline and at the end of program.  

All patients achieved meaningful functional gains. Improvements were not found using REY, RBMT or MFE measures. There were modest improvements in some scales of the CVIL.  

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

**Discussion**

In a recent study by O’Neil-Pirozzi et al. (2010), individuals with a TBI participated in 12 ninety 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 indicated significant differences between the groups and those with a severe TBI.
performed more poorly than those with a moderate injury. Those with severe TBIs, although they performed more poorly than those with mild or moderate injuries, did perform better than those in the control group who were individuals who had sustained a severe TBI. In all memory performance was seen to improve for all in the intervention group compared to the control group.

Thick-Penny and Barker-Collo (2007) randomly assigned 14 individuals to either the treatment or control groups. Those in the treatment group participated in a memory rehabilitation program. The memory groups consisted of 8 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 one month follow-up time period.

Sumowski et al. (2010) investigated the effects of retrieval practice (a technique that has been shown to be effective with non-TBI individuals) on those who had sustained a TBI. It has been shown with healthy individuals that retrieval practice allows for the retrieval of information shortly after it has been presented which leads to better delayed recall. Here 14 TBI and non-TBI individuals were presented with a series of paired words and divided across 3 learning conditions: massed restudy, spaced restudy and retrieval practice. Results indicate that retrieval practice was effective in improving memory in persons with a TBI.

Schefft et al. (2008) conducted two studies looking at the effect of a self-generation memory encoding strategy on memory. In both studies flash cards were presented to participants with a pair of words on each. In Study 1 subjects were assigned to either the generate condition or the read condition or vice versa. In the read condition cards were presented to the subjects with a pair of words on each card, which they were asked to read aloud. In the generate condition participants were asked to look at the word presented and voice the second word that had been on the card. In Study 2, pairs of words were presented to the participants followed by a cued recall trail or a free recall trial. Results of Study 1 indicate that memory test performance improved as a result of self-generation encoding procedures. Again the results of Study 2 indicated that self-generation strategy improved cued recall. It did not however improve free recall.

In a case series conducted by Hillary et al. (2003), 20 individuals with a TBI were presented with a series of words (4 groups of 20 words each). Each group was presented once (single condition), twice (massed condition) or twice with 11 words between each presentation (spaced condition). Spaced presentation led to significantly (p=0.018) greater recall and recognition of words than massed and once presented words. This result was also seen during delayed recall, and delayed recognition.
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).

Hux et al. (2000) examined the effect of training frequency on face-name recall. Seven TBI patients with demonstrated memory impairment in a modified multiple-baseline design utilizing 3 training phases (daily sessions, twice a week session and 5 times a day) participated in the study. The phases were counterbalanced, thereby eliminating any order effect. Daily sessions as well as twice a week sessions were found to be more effective than sessions that occurred 5 times a day. Mnemonics and visual imagery strategies were effective for 4 of the 7 participants regardless of frequency of intervention sessions.

Conclusions

There is Level 2 evidence indicating that memory-retraining programs appear effective, particularly for functional recovery although performance on specific tests of memory may or may not change.

There is Level 3 evidence supporting spaced retrieval practice as an effective method of improving memory post ABI.

There is Level 3 evidence suggesting that the spacing of repetitions improves memory post ABI.

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

Although several mnemonic strategies have been used to help improve memory post ABI, retrieval practice seems to be the most effective.

Recall and recognition of words can be enhanced by using a spaced learning
6.2.4 Cranial Electrotherapy Stimulation and Memory
Cranial electrotherapy stimulation (CES) is the application of less than 1 mA of electric current to the cranium. This application has been used to treat a variety of disorders, including treatment of withdrawal of patients with substance abuse (Michals et al. 1993). The effect of CES for the improvement of memory following brain injury was investigated.

Individual Studies

Table 6.12 Effect of Cranial Electrotherapy Simulation on Memory

<table>
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<tr>
<th>Author/Year/Country/Study design/PEDro Score</th>
<th>Methods</th>
<th>Outcome</th>
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<tr>
<td>Michals et al., (1993) USA RCT PEDro = 7</td>
<td>N=24 A double blind, sham controlled trial was performed on 24 brain-injured patients to evaluate the effectiveness of cranial electrotherapy stimulation (CES) on post-traumatic memory impairment. After a four-week study period, memory performance was measured using subtests from the Wechsler Memory Scale-Revised, California Verbal Learning Test, and Recurring Figures Test.</td>
<td>Results revealed that CES stimulation in brain-injured patients did not improve memory or immediate and delayed recall compared with controls. Repeated trial effects showed no significant differences between groups.</td>
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</table>

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

Discussion
Michals et al. (1993) studied cranial electrotherapy stimulation and its effect on post-traumatic memory impairment in clinical care patients with 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, from one RCT, that cranial electrotherapy stimulation did not help to improve memory and recall following brain injury.
Summary of Learning and Memory Post ABI
Not all patients respond equally to all intervention strategies and no study in the current review indicated whether severity of memory impairment (or memory profile) interacts with a particular external memory aid. 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 will are more likely to be used post injury. It was nuclear from the studies if any of the participants had had some knowledge of these appliances.

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. Pharmacologic intervention does not appear to be effective in improving learning and memory deficits.

6.3 Remediation of Executive and General Cognitive Functioning
6.3.1 Remediation of Executive 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 1983). 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 in contrast to typical unilateral insults following vascular injury. Not only direct contusion to the frontal and temporal lobes but also diffuse axonal injury sustained as a result of TBI affects executive functioning. TBI patients often present with cognitive and behavioral deficits in the presence of little physical impairment.

Cicerone et al. (2000) reviewed 14 studies dealing with executive functioning and problem-solving (Table 6.13). Only 3 of the identified studies were classified as a randomized controlled trial or non-randomized cohort study.

In the more current reviews by Cicerone et al. (2005; 2011) 9 and 18 additional studies 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”.

<table>
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<th>Table 6.13 Remediation of Executive Functioning</th>
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<tbody>
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<td>Cicerone et al. (2000)</td>
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<td>• Alderman et al., 1995</td>
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<td>• Burke et al., 1991</td>
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<td>• Lawson &amp; Rice 1989</td>
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<td>• Rebmann &amp; Hannon 1995</td>
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<td>• Youngjohn &amp; Altman 1989</td>
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<td>• Bieman-Copeland &amp; Dywan 2000</td>
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Executive function deficits are particularly relevant to brain injury survivors who tend to be younger (average age less than 40) 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).

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. The importance of evaluating effective interventions for treating executive dysfunction following brain injury is apparent since 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.

6.3.2 Group 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 is highly related to executive function and it is possible that programs and interventions aimed at improving community re-integration may in fact be focusing efforts on instrumental activities of daily living which may reflect (or are dependent on) executive functions.

Individual Studies

Table 6.14 Use of Group Therapy to Enhance Executive Function

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<tr>
<th>Author/Year/Country/Study design/PEDro Score</th>
<th>Methods</th>
<th>Outcome</th>
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<tr>
<td>Novakovic-Agopian et al., (2011) USA quasi RCT PEDro = 5</td>
<td>N=16 Participants were assigned to one of two groups (the goals-edu n=8 or the edu-goals group n=8). The goals training (goals-edu) group started with goal orientated attentional self-regulation, while the educational instruction (edu-goals) group began with brain health sessions. Each</td>
<td>Results of the first 5 weeks of training, showed those in the goals-edu group showed significant improvement (p&lt;0.0001) on the Attention and Executive Function summary domain and the memory domain (p=0.006), while those in the edu-goals group showed no</td>
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<td>Author/Year/Country/Study design/PEDro Score</td>
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<td>Ownsworth et al., (2008) Australia RCT PEDro = 9</td>
<td>N=31 subjects with an ABI were randomly assigned to 1 of 3 groups and each group had a weekly 3 hour session for 8 weeks. Group 1: group based support, Group 2: individual occupation support, Group 3: combined group and individual support interventions. The following measures were used to evaluate participants: Canadian Occupational Performance Measure (COPD); Patient Competency Rating Scale (PCRS); Brain Injury Community Rehab Outcome (BR-CRO 39); level of goal attainment was the primary outcome assessed.</td>
<td>change or minimal change. Following the change in groups, those in the edu-goals group, once they completed the goals training session showed significant improvement on the Attention and Executive Function Domain (p&lt;0.0001). Those in the goals-edu group who had completed the training session were able to maintain their gains. Following the completion of the goals training sessions all showed a decrease in task failures on complex functional tasks.</td>
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Data was analyzed over three time periods (pre, post and follow-up). When looking at the results of the pre-assessment data for each intervention group, no significant differences were noted on any of the measures: COPD, PCRS, BR-CRO and level of goal attainment (p>0.05). Looking at the satisfaction self ratings between pre and post assessment, an improvement was noted after each intervention (individual p<0.001; group p<0.025; combined p<0.01). Results indicated that at follow-up an improvement in self-rated satisfaction was noted for the group and combined interventions only (p<0.01). Results from the CPOM indicate that there was no significant difference between the group intervention pre to post comparison (p<0.028). A significant improvement was noted for the individual and combined interventions (p<0.01 and p<0.025 respectively) pre-post testing. Pre assessment and follow-up assessment for the relatives’ ratings of performance was significant for all three interventions (individual p<0.01; group p<0.01; combined p<0.025). Relatives’
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<td>Amos (2002) Australia RCT PEDro = 4</td>
<td>N=32 subjects (24 with ABI, eight without) were randomly assigned into three treatment groups: no treatment, external inhibition and increased stimulus salience. All treatment groups were compared to the normal controls. The Wisconsin Card Sorting Test (WCST) was employed to measure preservative error and random error.</td>
<td>There were no significant differences in total errors between groups, but groups differed significantly in total number of trials (p= 0.025), perseveration (p= 0.033) and categories achieved (p= 0.001). Comparisons between the unaided ABI group and the aided ABI groups and between the aided ABI groups and the control group showed that either aid significantly improved deficits in the ABI population on all measures. Comparisons between the inhibition and salience group revealed significance only for perseveration (p&lt; 0.045); the external inhibition group displayed much less.</td>
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<tr>
<td>Parente &amp; Stapleton (1999) USA Case-Control</td>
<td>N=32 A one year measure of TBI subjects with undefined etiologies participating in a group cognitive skills training module were compared to 64 TBI individuals who received services within the same time frame as the cognitive skills group (CSG) clients from the same rehabilitation centre.</td>
<td>10 of 13 CSG clients who completed the training program by the end of the year had maintained full employment for &gt; 60 days (76%) - versus 58% of the control group. Significance not calculated.</td>
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<tr>
<td>Ownsworth et al., (2000) Australia Pre-Post</td>
<td>N=21 chronic ABI subjects with adequate cognitive skills to communicate needs, understand information, possess an awareness of their difficulties and the motivation to change their lives participated in a 16-week group support program designed to improve self-awareness/regulation skills, and measure post-assessment mean score for emotional and behavioural problems was significantly lower (p&lt; 0.001), self-regulation skills improved significantly with no significant change in level of skills at 6 month follow up (p &gt; 0.10), level of psychosocial functioning improved significantly (p &lt; 0.001) with no</td>
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Evidence-Based Review of Moderate to Severe Acquired Brain Injury

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<th>Author/Year/Country/Study design/PEDro Score</th>
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<tr>
<td>Parente et al., (1999) USA Pre-Post</td>
<td>N=10 ABI subjects (mean age: 32 yrs; education 13 yrs) were given tasks that trained working memory for 1 hour between pre- and post test measurement (Digit span task, letter/number sequencing tasks from WAIS-III. Control clients matched to treatment group by sex and chronicity.</td>
<td>significant change at 6 month follow up (p &gt; 0.30).</td>
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PEDro = Physiotherapy Evidence Database rating scale score (Moseley et al., 2002).

**Discussion**

In a current RCT Novakovic-Agopian et al. (2011) randomly assigned 16 individuals either a goals training (goals-edu) group or an educational instruction (edu-goals) group. The goals training program had 2 components: the first emphasized mindfulness-based attention-regulation training, and the second emphasized patient’s defined goals. Training involved ten 2 hour sessions of group training, 3 individual 1-hour session and 20 hours of home practice over a 5 week period. An example of training included the implementing a calendar or organizational system to increase completion of assignments or tasks. At the end of the five week period the groups reversed roles. Both groups were assessed at baseline, at the end of the first 5 weeks and again at the end of the 10th week. Those in the goals-edu group showed significant improvement on the Attention and executive Function summary domain compared to the edu-goals group. At the 10th week evaluation time period, the edu-goals group, once they had completed the training sessions also showed improvement and the goals-edu group continued to show improvement even though they were no longer receiving the intervention (Novakovic-Agopian et al., 2011).

In an earlier RCT Ownsworth et al. (2008) randomly assigned individuals to one of three groups. All were evaluated pre and post intervention then again at the 7th month follow up. Overall, when looking at the baseline measures, they found no significant differences on the performance self-ratings, satisfaction self-ratings, relatives’ performance ratings, and relatives’ satisfaction ratings (p>0.05) for the groups. The satisfaction self-ratings between pre and post assessment, indicated an improvement after each intervention (individual p<0.001; group p<0.025; combined p<0.01). At follow-up an improvement in self-rated satisfaction was noted for the group and
combined interventions only (p<0.01). Results from the CPOM indicate that there were no significant differences when looking at the scores from the group intervention pre to post comparison. Significant improvement was noted when looking at the scores for the individual and combined interventions (p<0.01 and p<0.025 respectively). Pre assessment and follow-up assessment for the relatives’ ratings of performance was significant for all three interventions (individual p<0.01; group p<0.01; combined p<0.025). Relatives’ ratings of satisfaction (pre and post) found a significant improvement for the individual (p<0.025) and combined (p<0.01) interventions but not for the group intervention (p<0.117). A look at the psychosocial outcomes for each intervention group showed few significant differences.

Ownsworth et al. (2000) studied the effect of group therapy aimed at improving self-regulation skills as well as psychosocial functioning for brain injury survivors greater than 1 year post injury. Self-regulation was evaluated using the self-regulation skills interview which examines how brain injury survivors would handle self-identified difficulties (Ownsworth et al., 2000). Both self-regulation abilities and psychosocial functioning improved following the treatment intervention and improved performance was maintained at 6 month follow up.

Parente and Stapleton (1999) in a descriptive study 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.

Parente et al. (1999) also studied retraining of working memory post traumatic brain injury. Although working memory would at first glance appear to be a primarily memory related brain function, the authors describe the concept of working memory as involving three main elements. These elements are the articulatory loop which hold verbal information, the visuospatial sketchpad which stores and interprets visual information and the executive system which organizes, prioritizes and allocates information processing resources. In this pilot study, 10 subjects were assigned to the intervention group who completed tasks to enhance working memory functioning between testing sessions. The testing sessions were only 1 hour apart. A control group matched for age, gender and injury type completed the same testing without training. The results showed
A significant improvement for the letter number sequencing task for the intervention group, however there was no difference between groups on digit span task performance.

Amos (2002) completed a RCT that evaluated remediating deficits of switching attention in patients with acquired brain injury. Twenty-four patients with ABI were randomly assigned to one of three groups and compared to eight normal controls. Results suggest perseverative error and random error are separate functions when switching attention, as suggested by a neural network model. The author notes that external inhibition significantly reduced perseverative error (applying an inappropriate rule continually), while an increase in perceptual salience decreased random error (continually failing to apply an appropriate rule) on the WCST.

Fins et al. (1995) using three single case studies, examined the need for developing team cooperation procedures to treat patients following brain injury. Results indicated that overall, there was a slight tendency, although minimal, toward improvement on the 10-questions task. With the assignment task however, a considerable amount of variability was revealed.

**Conclusions**

*There is conflicting evidence supporting the use of group-based interventions to treat executive dysfunction post ABI.*

**Group cognitive interventions may be effective for improving executive function: however more research needs to be completed to determine what the effectiveness is.**

**6.3.3 Goal Management Training**

With regards to cognitive rehabilitation, much of therapy is patient goal directed with both long and short term goals often identified (Carswell et al., 2004). The ability to manage goals is often emphasized as a component of brain injury community reintegration programs and is integral in the completion of instrumental activities of daily living.
**Individual Studies**

Table 6.15 Goal Management Training in Brain Injury Rehabilitation

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<tr>
<th>Author/Year/Country/Study design/PEDro Score</th>
<th>Methods</th>
<th>Outcome</th>
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<tr>
<td>Levine et al., (2000) Canada UK RCT PEDro=4</td>
<td>N=30 Subjects with moderate to severe ABI as indicated by GCS and PTA were randomized into Goal Management Training (derived from Duncan's theory of goal neglect on disorganized behaviour following TBI) and a Motor Skills Training groups.</td>
<td>Although both groups improved, GMT was associated with significant gains on everyday paper-and-pencil tasks designed by the authors to mimic problematic tasks for patients with goal neglect (p&lt;0.05).</td>
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<tr>
<td>Walker et al., (2005) Australia Pre-Post</td>
<td>N=11 Individuals (mean time since injury of six years; average age of 30 years; nine men and two women) with severe to extremely severe brain injury (average 11 weeks PTA) participated in a community-based, goal-planning programme over a period of 18 months. The first 9-months of the programme was spent raising funds for a 9-day outdoor adventure course. Following the course, the participants met for 4-months and focused on goal achievement and problem-solving tactics.</td>
<td>All participants completed the three stages of the programme. 81% of identified goals were achieved. All but one participant achieved at least one goal. There were no significant differences noted between pre- and post-treatment scores on the Depression, Anxiety Stress Scales (DASS), General Well-Being Schedule (GWB), and the European Brain Injury Questionnaire (EBIQ) on the Wilcoxon Signed Ranks Test, although all changes were in direction of improved psychological health.</td>
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</table>

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

**Discussion**

Levine et al. (2000) completed a RCT comparing a group of patients taking goal management training strategies to a control group who were 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.

Walker et al. (2005) conducted an alternative goal planning, cognitive rehabilitation programme focusing on the development and achievement of goals following brain injury. This single group intervention involved three phases: (1) nine-months of planning and fund-raising for an outdoor adventure course; (2) a nine-day outdoor course; and (3) four-months following the course, the participants focused on goal achievement and problem-solving skills. More than 80% of the identified goals of participants were achieved. No significant pre- and post-treatment differences were noted on psychological measures: Depression, Anxiety Stress Scales (DASS), the General Well-Being Schedule (GWB), and the European Brain Injury Questionnaire (EBIQ). This
programme demonstrated a unique and challenging, community-based intervention for group goal management following brain injury.

**Conclusions**

*There is Level 2 evidence, based on a single RCT, that goal management training is effective for improving paper and pencil everyday tasks and meal preparation skills for persons with an ABI.*

*There is Level 4 evidence, based on a single group intervention, that goal planning in the form of leisure activities is effective for achieving identified goals following injury.*

**Goal management training is effective for treating some executive function deficits.**

**Summary of Executive Function**
The current studies support the notion that group cognitive interventions may be effective for improving executive function. Parente and Stapleton (1999) provide some limited evidence that efforts to improve executive function may have potential to improve chances for future competitive employment. There is also some evidence that pharmacological intervention, amantadine, may be effective in improving executive function. Evidence supporting the use of bromocriptine is inconclusive. Ultimately, further research is required to determine which methods are most effective for improving executive function.

**6.3.4 Remediation of General Cognitive Functioning**
Intervention for treatment of cognitive deficits post traumatic brain injury tend to be diverse with variability between the interventions themselves and the outcome measures used to document results. For the purposes of this section, interventions were included that either targeted multiple cognitive domains such as attention, memory, information processing speed, executive functions and visuoperceptual function or were non-specific with regards to intended outcome. For example, a general cognitive rehabilitation program would tend to document outcomes across multiple domains.

**6.3.4.1 Cognitive Rehabilitation Strategies**
Gordon et al. (2006) conducted an extensive review of the traumatic brain injury rehabilitation literature and identified 13 studies dealing with rehabilitative treatments of cognitive deficits (Table 6.16). A comprehensive literature search of MEDLINE, CINAHL, and PsychINFO databases was performed. Studies included in this review had a
multitude of inclusion criteria. 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., 2008; Sohlberg et al., 2003b). Studies included in this section have examined the effects of cognitive rehabilitation strategies.

Table 6.16 Rehabilitative Treatment of Cognitive Deficits

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<th>Author/Year/Country/Study design/PEDro Score</th>
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<td>Vas et al., (2011) USA RCT PEDro = 6</td>
<td>N=28 Subjects were randomly assigned to 1 of 2 groups: Top down SMART group (exp group) and the information based BHW (control group). A comparison of the benefits of the two groups was conducted. Training was offered for a total of 18 hrs during 12 group sessions over an 8 week period. The first 15 hrs took place over the first 5 week, 10 sessions (2/week). The remaining 2 sessions took place over the remaining 3 weeks (booster sessions). Each SMART session covered various topics which were discussed by participants. Homework assignments were also given to prepare participants for the next session. BHW sessions were designed to be information based sessions covering everything from brain anatomy to health life style and cognitive changes. Reading assignments were also given each week. Pre, Post and Following treatment, results indicate that those in the SMART group showed significant improvement on GIST reasoning (p=0.03) on the community integration questionnaire (CIQ) (p=0.02) and the working memory (listening span task) (p&lt;0.001) compared to the BWH group. Pretraining scores were similar for the groups. Those in the SMART group showed significant improvement on 3 executive functions following training (inhibition, nonverbal reasoning, and cognitive flexibility). Overall SMART was found to enhance gist reasoning, of which the benefits were seen in other domains (listening span and increased participation). Six months later the benefits were still evident.</td>
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<td>Author/Year/Country/Study design/PEDro Score</td>
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<td>Post testing was conducted (3 weeks prior to session beginning, 3 weeks following sessions completing and 6 months post session completion). The examiner was blinded to the group each participant was assigned to.</td>
<td>On the domain of attention and executive functions, all (n=12) in goals training showed an increase from pre to post goals training while only 7 of 12 showed an increase from pre to post education. Performance scores increased significantly after the goals training sessions compared to the education sessions. For the group that began in the education session, scores were also found to improve significantly in the post goals training compared to the education training. Tests of motor speed of processing showed no significant differences between the two interventions.</td>
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<td>N=12 Participants were randomly assigned to 1 of 2 groups and at the end of the 5th week they began the alternative intervention. Two interventions were used: goals training and education. The goals training protocol was based on a goal management training intervention. Participants attending 10 2 hrs sessions of group based training, 3 individual 1hr training sessions and 20 hrs of home practice over 5 weeks.. The education program was a 5 week didactic educational instruction regarding brain injury.</td>
<td>Test on recall occurred twice. The first time was after a short delay and the second time was after a longer delay. No significant differences were seen after the short delay; however, after the longer delay, recall was significantly better after using the modeling technique.</td>
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<td>N=16 Participants were randomly assigned to either the modeling or moulding group. All learned hand movement sequence A during their first learning trial and hand movement B during their second. The moulding technique involved a hand over hand technique and the modeling technique had the participant copy the experimenter.</td>
<td>Treatment group showed significant improvement in problem-solving (WCST, PSI, PSQ) and emotional self-regulation (PSQ), objective observer ratings of role-play scenarios (PSRPT), visual memory (immediate recall- WMS III: p &lt; 0.001), self-esteem (RSES: p&lt; 0.05), fewer perseverative responses (WCST: p&lt; 0.05), gains in PSI total score (p = 0.005), PSQ Clear Thinking and Self-Regulation (p = 0.01 and p&lt; 0.05), and PSRPT (p&lt; 0.005).</td>
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<td>N=46 Subjects with mild to severe TBI (mean age: 43.6 yrs; mean chronicity: 48.2 mths) with a higher level of functioning were randomized into two groups, the first of which received 1 individualized 2 hr session / week for 24 weeks of a group treatment protocol (emotional self-regulation strategies, problem solving skills) and the second a conventional neuropsychological rehabilitation program.</td>
<td>Control improved significantly in the</td>
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<td>Author/Year/Country/Study design/PEDro Score</td>
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<td>Watson et al. (2000) USA RCT PEDro = 7</td>
<td>N=120 Active military personnel with TBI from a moderate to severe closed head injury randomly assigned to an intensive in-hospital cognitive rehabilitation program or a control group (limited at home rehabilitation) as it effects return to gainful employment and fitness at 1 year follow-up.</td>
<td>Watson-Glaser Critical Thinking Test (p&lt; 0.05), suffered significantly reduced somatic symptoms (p&lt; 0.005), less severe cognitive symptoms after PCL (p&lt; 0.05), significantly improved emotional self-regulation skills (PSQ Self-Regulation: p&lt; 0.01). Both groups improved on Logical Memory immediate recall, as well as Logical Memory and Visual Memory delayed recall.</td>
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<td>Salazar et al. (2000) USA RCT PEDro = 7</td>
<td>N=14 Those in Condition A (n=7) received 24 hours of attention process training (APT), in 3 one-hour sessions each week for a total of 10 weeks. Attention process training is a cognitive rehab program that has been used to remediate attention deficits following an ABI. Tasks chosen for each subject were specific to his or her needs. Tasks were designed to place increasing demands on complex attentional control and working memory. Those assigned to Condition B (n=7) received a combination of brain injury education, supportive listening and relaxation training. Sessions ran for 10 weeks, one hour per week. All subjects worked directly with a therapist for the length of the study. Following therapy subjects were assessed using various scales (Paced Auditory Serial Addition Task (PASAT), Gordon Diagnostic Vigilance and Distraction, Controlled Oral Word Association Task (COWAT)) and interviews.</td>
<td>No significant differences between cognitive, behavioural or quality of life measures (p= 0.51).</td>
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<td>Sohlberg et al., (2000) USA Pedro = 8</td>
<td>N=30 TBI subjects with moderate or severe injury as determined by GCS on admission, randomly assigned to remedial (without Pre/post test measured by computer based visual processing, data entry and recording tasks. Weekly measures of 2</td>
<td>Those in the APT group reported significantly more changes following intervention then those in the brain injury education group (p&lt;0.05). The greatest number of changes was reported in attention and memory than in psychosocial functions. Changes in PASAT scores were greater for those who reported more than 2 cognitive changes. Results of the PASAT also found that those with higher levels of vigilance had higher PASAT scores. Those with higher vigilance scores had higher COWAT scores.</td>
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<td>RCT PEDro = 4</td>
<td>Instruction) and compensatory strategy (verbalization, chunking and pacing) intervention groups receiving a 45-minute session once a week for 4 weeks.</td>
<td>computerized matching tasks and the PASAT. Pre/post and weekly tasks significantly improved in both groups (p&lt;0.01). No significant improvement due to intervention (p&gt;0.05).</td>
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<tr>
<td>Neistadt et al., (1992) USA RCT PEDro = 6</td>
<td>N=45 Male subjects were randomly allocated to one of two treatment groups: (1) the Adaptive Functional Training; or (2) Remedial Perceptual Skills Training. The Parquetry Block test, Block design subtest of the Wechsler Adult Intelligence Scale-Revised (WAIS-R) and the Rabideau Kitchen Evaluation-Revised (RKE-R) was assessed pre- and post treatment.</td>
<td>After treatment, the remedial group improved significantly more than the adaptive group on the Parquetry Block test (p= 0.0185), but there were no significant differences on the WAIS-R Block Design subtest. 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.</td>
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<td>Johansson and Tornmalm (2012) Sweden Cohort</td>
<td>N=18 Treatment consisted of a computerized training program (Cogmed QM), coaching, education and peer support. The computerized training program was designed to train working memory. Visual and auditory working memory tasks are given and the difficulty level was automatically adjusted to the individual and past performances. Groups participating consisted of 4 to 6 individuals who attended 3 sessions per week for 7-8 weeks. Coaching was provided by trained staff throughout the training.</td>
<td>Training sessions ranged from 20 to 25, with all participants completing the training. Results of the Cognitive failures questionnaire (CFQ) showed a significant reduction of cognitive problems for all participants. The Canadian Occupational Performance Measures (COPM) also showed significant improvement on both performance (&lt;0.01) and satisfaction with performance (p&lt;0.05).</td>
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<tr>
<td>Cicerone et al., (2004) USA Non-RCT</td>
<td>N=56 moderate to severe TBI subjects&gt; 18 years, able to communicate verbally, and accompanied by family member, were divided into a standard neuro-rehabilitation (SRP – 2 hrs/ day; 3x/week focused on executive, meta-cognitive functioning and interpersonal process) control (n=29) and an intensive cognitive rehabilitation (ICRP – 5 hrs / day, 4x/week in small groups emphasizing awareness, compensation, communication skills, family support and work trials) treatment (n=27) group.</td>
<td>Although both groups improved significantly on the CIQ following treatment (p&lt;0.001), IRCP group showed greater improvement when time is factored in (p= 0.021) and significant improvements in overall neuro-psychological (NP) functioning (p&lt;0.001). Participants who showed an significant improvement on the CIQ showed a greater improvement on overall NP functioning (P=0.001).</td>
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<td>Miotto et al., (2008)</td>
<td>N=30 individuals with lesions in the frontal lobe were included in the following study.</td>
<td>Results indicate that all three groups showed improvement on executive</td>
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<td>United Kingdom Quasi-RCT</td>
<td>Subjects were placed in one of three groups (with the first half of participants being randomized to a group and the second half being placed into one of the 3 groups). Group 1 (n=10) received the attention and problem solving intervention. Group 2 (n=10) received weekly sessions of attention and problems solving training by 2 psychologists (1 x per week for 90 minutes). Group 2 also received further information and education interventions (an information booklet containing information on brain injury, cognitive, behavioural and social consequences and a list of suggested cognitive exercises. Group 3 received usual treatment (PT, OT etc). Function regardless of the intervention or treatment they received. On assessments 1 and 2 groups 1 and 2 showed significant improvement (P=0.023 and p=0.014 respectively). The change in scores for group 3 did not quite reach significance (p&lt;0.059). Results for the VIP test also showed improvement but again no significant differences were noted between the three groups. A comparison of the results from assessment 2 to assessment 3 did show significant improvement, on each scale; however there were no significant differences between the groups.</td>
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<td>Turkstra (2008) USA Case-Control</td>
<td>N=38 All participants (cases (TBI) n=19, and control (typically developing) n=19) were asked to complete the Reading the Mind in the Eyes Test – assessing the subjects ability to read an individuals thoughts by looking at his or her eyes; the Video Social Inference Test (VSIT) – video vignettes used to assess social inferences; and the Competing Language Processing Test (CLPT) – a working memory test. All participants completed the tasks listed in random order. A between group comparison was conducted looking at the scores of all the tests. Results of CLPT (True/False and words recalled) test indicated the controls significantly scored higher than cases (p&lt;0.05, p&lt;0.001 respectively). Scores on the VSIT also found the controls performing significantly better than cases. When looking at the scores on the social inference items, requiring individuals to make predictions on future behaviours, no significant differences were noted between groups (p&gt;0.05).</td>
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<td>Ownsworth et al., (2006) Australia Single subject intervention</td>
<td>N=1 The 36 year old male participated in a 16 week program that targeted error awareness at home (while cooking) and at his volunteer job. Subject was 4 yrs post injury when treatment began. The program was described as a metacognitive contextual intervention. During the four week baseline period, subject made 21 errors while participating in the cooking task and self corrected only 15% of the time. During the 16 week treatment period, the subject self corrected 27% of his errors; however, the maintenance period saw the subject self correct 46% of his errors. It was noted that the subject would always need a certain amount of prompting and supervision when cooking.</td>
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<td>Boman et al., (2004) Sweden</td>
<td>N=10 Each participated in an individual cognitive training session for 1 hr/3x a week for 3 weeks at home or work. The program For the following: sustained attention, selective attention and alternating attention significant changes (p&lt;0.05,</td>
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<tr>
<td>Author/Year/Country/Study design/PEDro Score</td>
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<td>Pre-Post</td>
<td>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. Digit Span Test, Claeson-Dahl test; Rivermead Behavioural Memory test (RBMT), Assessment of Motor and Process Skills, European Brain Injury Questionnaire.</td>
<td>P&lt;0.05, p&lt;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 month follow up. Score increases (p&lt;0.05) on the RBMT were found at the 3 month follow up compared to the RBMT scores at the pre test. When looking at changes in the RBMT score pre to post training, changes were not found. 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</td>
</tr>
<tr>
<td>Brett &amp; Laatsch (1998) USA Pre-Post</td>
<td>N=10 TBI high school students (14-18 years, chronicity 1-16 years) with borderline or above intelligence who participated in an individualized, bi-weekly session (40 minutes) of computer administered Rehabilitation Therapy (CRT) based on a 3 level developmental model of cognitive rehabilitation. Pre and post treatment evaluations measured General intellectual functioning, self-esteem, concentration/sensory processing, memory and problem solving.</td>
<td>Significant improvement in memory skills (WRAML screen: p=0.025); no significant differences found in any other measure.</td>
</tr>
<tr>
<td>Serino et al., (2007) Italy Case Series</td>
<td>N=9 Individuals with a mean GCS of 10 were selected for participation in the following study. All had severe working memory (WM) deficits and underwent working memory training (WMT). The WMT was based on the repeated administration of the Paced Auditory Serial Addition Test (PASAT). 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 (e.g., 5 6 “respond 11”, 6 “respond 12” 3 “respond 9”). Two additional tests (the Months tasks and the Word tasks) were also administered in a similar way. During the Months task, a sequence of months names was presented auditorily to the participants, one at a time. Patients were asked to say out loud which month</td>
<td>Study results indicate the greatest improvement in performance occurred from the intermediate to the final sessions (p&lt;0.0005) after the WMT. Improvement from the initial to intermediate sessions did not show any significant improvement in working memory (p&lt;0.46) after GST. Working memory (p&lt;0.05), divided attention (p&lt;0.05), executive function (p&lt;0.05), and long term memory (p&lt;0.05) for subjects were significantly improved in the final session compared to the intermediate session. The same was not noted on the speed processing and sustained attention tasks (p&gt;0.05). Working memory training tasks were also found to improve scores on</td>
</tr>
</tbody>
</table>
came first (e.g., January & June, January comes first etc). Administration of the Words test was similar. During general stimulus training (GST) patients were provided with a description and an explanation of their cognitive impairments in an effort to increase their awareness of their deficits and disabilities. 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.

### Laatsch et al., (1999) USA Case series

<table>
<thead>
<tr>
<th>Author/Year/Country/Study design/PEDro Score</th>
<th>Methods</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>N=5 Individuals with mild to moderate TBI between 18 and 65, 2-48 months post injury received a mean of 15.8 (range 6-36) individualized cognitive rehabilitation sessions (CRT – meta-cognitive approach). Progress was measured by a battery of NP tests prior to, at completion and 3-12 months post treatment.</td>
<td>various psychosocial outcomes.</td>
<td>NP measures: WAIS-R, WMS-R, CVLT, RCFT, SCWT, WCST or ACT, SPECT image. 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.</td>
</tr>
</tbody>
</table>

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

### Discussion

In a 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 (SMART) group or the Brain Health Workshop (BHW) group. Each groups received 15 hours of training over an eight week period. Those in the SMART 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 SMART 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 BHW group participated in information sessions. Sessions for the BHW 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 SMART group showed significant improvement on gist reasoning and measures of executive function.

Chen et al. (2011) in a recent study, randomized a group of individuals (n=24) who had sustained a TBI, into one of two groups: a goals training group (n=12) and an education
group (n=12). Those in the goals training program (the experimental condition) was based on a goal management training program. Participants attended ten 2 hour sessions of group based training, 3 individual 1 hour training sessions and 20 hours of home practice over 5 weeks. The control group attended a five week didactic educational instruction regarding brain injury. Following training, performance on tests of attention and executive control increased for 100% of participants in the experimental condition, while only 58% in the education groups showed an increase in test scores. On tests looking at learning and memory performance scores increased for 92% (11/12) of those in the goals training program and 33% (4/12) in the education program.

In a study investigating the effects of two instructional techniques modeling and moulding 16 participants were instructed to learn a sequence of 7 hand movements in the correct order (Zlotowitz et al., 2010). In the moulding condition, participants were taught the hand movements using a hand over hand technique. The modeling condition had participants model the hand movements as presented by the experimenter. Participants on tested on recall 5 minutes after their sequence recall and 30 minutes later. Results indicated there was no difference between the techniques after the short delay recall; however, after the longer delay, recall was significantly better after the modeling condition compared to the moulding condition (Zlotowitz et al., 2010).

In a randomized controlled trial by Dirette et al. (1999) although there were significant improvements on post intervention results for both intervention and control groups, there was no overall difference between groups when the experimental group was taught to use compensation strategies including verbalization, chunking and pacing. In this study, the authors did note that control participants spontaneously relied upon compensatory strategies, which may have accounted for improvement.

Rath et al. (2003) 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.

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. Outcomes for the effect of treatment on functional test performance revealed a trend as predicted, although non-significant, toward the functional group improving more than the perceptual skills group. Training-specific learning appears to be an effective approach to rehabilitation as demonstrated by the treatment effect.

In a recent prospective cohort study, Johansson and Tornmalm (2012) looked at the benefits of a working memory program on 18 individuals who had sustained either a TBI or had had a stroke resulting in moderate to severe cognitive deficits. The working memory training program used the 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 6th month follow up.

Cicerone et al. (2004) compared an intensive cognitive rehabilitation program to a standard rehabilitation program. This intensive program included individual and group therapy 4 days per week for 5 hours per day for a total of 16 weeks. The main outcome for this study was community integration post injury. The treatment group had a significantly better outcome compared to the control group. With regards to cognitive outcomes, analysis was not performed on the control group due to incomplete data; however, there was a significant improvement on post intervention composite neuropsychological scores for the treatment group who on average were greater than two years post injury at the start of the intervention.

In another RCT conducted by Sohlberg et al. (2000) they found that those who were assigned to the attention process training group (APT) (n=7), showed improved performance on cognitive function and executive attention tasks compared to than those in the brain education therapy group (n=7). Results of the Paced Auditory Serial Addition Task (PASAT) found those with higher PASAT scores were related to higher levels of vigilance. Improvement in PASAT scores was greater after APT than in brain education, suggesting subjects benefited more from APT than from the brain education program. Similar results were also found when looking at the scores of the Controlled Oral Word Association Task (COWAT- a measure of frontal function). Those with higher vigilance scores had higher COWAT scores. Self-reports of those receiving only brain education, indicate an improvement in psychosocial function.

In an effort to improve the central executive system of working memory, Serino et al. (2007) invited nine subjects to participate in a working memory training (WTM) program. Treatment was based on the repeated administration of the Paced Auditory Serial Addition Test (PASAT), and two tasks derived from the PASAT and Months and
Words Task. The difficulty of each task was varied. The results of the working memory test were compared to a general stimulus training (GST) program which was also provided to all subjects. The GST used the same material used for the WST tasks; however, when this material was used in the GST the tasks only required basic level attentional demands. The results indicate the GST had no significant impact on the performance of subjects compared to the WMT. Results from the WMT showed improvements in working memory, divided attention, executive functions, and long term memory. These results support the use of WST in recovering the central executive system impairments.

Laatsch et al. (1999) examined individual cognitive rehabilitation therapy using a metacognitive approach with the five participants with mild to moderate traumatic brain injury receiving between six to 36 one-hour sessions. The results demonstrated improvement in cognition for tests of intelligence, memory, processing speed and problem solving, however statistical results were not reported. The results also demonstrate a statistical significant increase in cerebral blood flow on SPECT imaging following cognitive rehabilitation intervention.

Brett and Laatsch (1998) studied the effects of a cognitive rehabilitation therapy program for TBI survivors in a high school setting. The intervention included biweekly 40-minute sessions for a total of 20 weeks. Cognitive therapy focused on alertness, attention, concentration, perception and memory as well as problem solving. Only memory demonstrated a statistically significant improvement post intervention whereas general intellectual functioning, concentration and problem solving did not demonstrate significant improvement.

In a quasi-experimental study conducted by Miotto et al. (2008) 30 patients were placed (15 were randomly assigned to a group) in one of three groups: group 1 (n=10) received the attention and problem solving intervention; group 2 (n=10) received weekly sessions of attention and problems solving training by 2 psychologists (1 x per week for 90 minutes) along with information and education interventions and a list of suggested cognitive exercises; while group 3 received usual treatment (PT, OT etc). Results indicate that all three groups showed improvement on executive function regardless of the intervention or treatment they received. Groups 1 and 2 showed significant improvement (p=0.023 and p=0.014 respectively) on assessment one and two, whereas the change in scores for group 3 did not quite reach significance (p<0.059). Results for the VIP test also showed improvement but again no significant differences were noted between the three groups. A comparison of the results from assessment 2 to assessment 3 did show significant improvement, on each scale; however there were no significant differences between the groups. Overall although improvement was noted
for groups 1 and 2, group 3 also showed signs of improvement without any added intervention.

Turkstra (2008), in a between groups comparison study (n=38) found those with a TBI did not perform as well as those without an injury on various cognitive/communication tests. Results of CLPT (True/False and words recalled) and the VSIT test indicated that the controls significantly scored higher than the clinical group. No significant differences were noted between groups (p>0.05), when looking at the scores on the social inference items.

In the single subject intervention study conducted by Ownsworth et al. (2006), they found that by exposing their subject to systematic feedback they were able to reduce the number of errors made while engaging in cooking tasks and volunteer work. During the baseline phase the subject was videotaped performing various tasks. Upon viewing the tapes, it was noted the subject made 21 errors but during the treatment phase of the study a 46% decline in errors was noted. This reduction in errors was noted during both the cooking tasks and volunteer work completed by the subject.

Boman et al. (2004) in a study of 10 individuals with mild or moderate TBI, after completing 1 hour of an individual cognitive training 3 times a week for 3 weeks, significant improvement was noted on the attention processing training test in sustained attention (p<0.05), selective attention (p<0.05), and alternating attention (p<0.01) pre to post training and at 3 month follow-up. Scores on the RBMT were also seen to have significantly increased at the 3 month follow-up compared to pre test scores (p<0.05). Changes on the Claeson-Dahl Memory test did not increase pre to post to 3 month follow-up.

Salazar et al. (2000) in a RCT of 120 moderate to severe TBI patients studied the efficacy of an intensive, eight-week, in-patient cognitive rehabilitation program compared to a limited home rehabilitation program with weekly telephone contact from a psychiatric nurse. Overall there were no differences between groups with regards to return to work or fitness for duty at one-year. There were also no differences in cognitive, behavioral or quality of life outcomes.

Cicerone et al. (2000) had concluded that comprehensive-holistic cognitive rehabilitation should be recommended as a practice guideline for patients with either a stroke or acquired brain injury. Since completion of this review, further quality studies have been published supporting a general cognitive therapy approach following acquired brain injury. In the studies by Dirette et al. (1999) Rath et al. (2003) and Cicerone et al. (2004) comparisons of specific strategies using experimental techniques (randomized and non-randomized) are attempted. All groups demonstrated benefit
from the interventions and in the studies by Rath et al. (2003) and Cicerone et al. (2004) there were overall trends to improvement for the experimental groups. The study by Salazar et al. (2000) provides contradictory results to these other studies in that no benefit was demonstrated for an intensive in-patient rehabilitation program versus a limited home based rehabilitation program. This study was a RCT and challenges the trend of studies demonstrating the benefit of intensive cognitive rehabilitation programs. Comparison of cognitive rehabilitation strategies against a non-intervention group has been generally considered unethical supporting the general held belief that cognitive rehabilitation is effective, therefore trials such as these comparing different cognitive therapy strategies remain necessary to optimize rehabilitation outcomes.

Although there are differences in the delivery techniques of cognitive rehabilitation therapy, most studies when considering within-group comparisons demonstrated an overall improvement in cognitive abilities across multiple cognitive domains. The majority of the studies included patients greater than one-year post injury, which would assist in controlling for the effects of spontaneous recovery. There are limitations in most studies in that typically a time series design is used with pre- and post-intervention testing where the subject acts as their own control. The primary limitation with regards to brain injury rehabilitation is time-dependent confounding. Two factors contribute to this including anticipated spontaneous recovery as well as the consideration of the practice/ learning effect of repeat neuropsychology testing which may lead to higher scores.

Analysis of findings from the current review as well as those from Cicerone et al. (2005) and Gordon et al. (2006) all suggest that future studies need to control for patient characteristics (e.g., level of impairment needs to be clearly defined, not just severity of injury), spontaneous recovery and practice effects on outcome measures used. Studies should not just rely on psychometric tests but should consider functional outcome measures and long-term effects of treatment interventions should be monitored through follow-up.

Conclusions

There is conflicting evidence as to the effectiveness of cognitive rehabilitation programs focusing on memory strategies and selective attention.

There is Level 2 evidence that general cognitive rehabilitation therapy post acquired brain injury is effective for improving cognition. Although there are variable strategies and protocols for cognitive rehabilitation, all comprehensive interventions appear to provide benefit.
There is Level 4 evidence that working memory training is effective in recovering the central executive system of working memory.

There is Level 4 evidence that an outpatient day program is effective for assisting brain injury survivors in returning to competitive employment.

Programs focusing on memory strategies and selective attention post ABI have not been shown to be effective.

Outpatient day programs are effective in helping survivors of a brain injury return to competitive employment.

6.4 Pharmacological Interventions to Assist with Cognitive Recovery Post ABI

6.4.1 Donepezil
The effectiveness of the cholinesterase inhibitor, Donepezil, for improving cognitive functioning and memory dysfunction following brain injury has been assessed. Memory dysfunction following an ABI is a common occurrence. The long term impairment of an ABI affects a person’s ability to return to work, school and it can affect their ability to live alone (Katz et al., 1989). According to Zhang et al. (2004), pharmacologic intervention using a cholinergic agonist to help facilitate cognitive deficits following TBI had not been studied previously; however, when tested with individuals who have been diagnosed with Alzheimers, donepezil has been found to be useful in treating memory problems (Walker et al., 2004; Morey et al., 2003).

Individual Studies

Table 6.18 Effect of Donepezil on Memory and Cognitive Functioning

<table>
<thead>
<tr>
<th>Author/Year/Country/Study design/PEDro Score</th>
<th>Methods</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Zhang et al., (2004) USA RCT PEDro = 7</td>
<td>N=18 Individuals with a history of TBI of any severity with attention or short-term memory impairments as shown by WMS III, and PASAT were randomly assigned to treatment group A (received donezepil orally for 10 weeks, followed by a 4 week washout period, followed by Group A (donepezil phase) showed significant improvement over group B (placebo phase) on immediate auditory (p=0.002) and visual memory (p&lt;0.001) measures of WMS-III and PASAT (p&lt;0.001) at wk 10. Increased scores in Group A were continued following washout. Group B</td>
<td></td>
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<tr>
<td>Author/Year/ Country/Study design/PEDro Score</td>
<td>Methods</td>
<td>Outcome</td>
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<tr>
<td>Khateb et al., (2005) Switzerland Case Series</td>
<td>N=10 Individuals who had sustained a moderate or severe TBI who received 5 mg/day for 1 month, followed by 10 mg/day for 2 months. The following assessments were completed: Affective &amp; Behavioural assessment (HAD &amp; DEX questionnaire), Neuropsychological Evaluation (executive functioning, learning and memory and attention) outcome measurements and analysis.</td>
<td>Improved following donepezil phase (wk 24) – but inter-group comparisons were not significant (audio: p=0.588; visual: p=0.397, PASAT presentation rates p=0.545, 0.12, 0.783, 0.410) due to Group A’s sustained high scores.</td>
</tr>
<tr>
<td>Morey et al., (2003) USA Case Series</td>
<td>N=7 Single subject ABAC design with patients (5 males and 2 females) who received 5-10 mg/day of donepezil (Aricept). Each participant served as his/her own control. Repeated measures analysis of variance was used.</td>
<td>Significant improvements in immediate and delayed memory were found when taking 10 mg/day of Aricept, as measured by the Brief Visual Memory Test-Revised.</td>
</tr>
<tr>
<td>Masanic et al., (2001) Pre-Post</td>
<td>N=4 Sixteen-week open-label study of patients with chronic, severe TBI who were given donepezil 5 mg daily for 8 weeks followed by donepezil 10 mg daily for 4 weeks.</td>
<td>Mean scores for short-term and long-term recall on the Rey Auditory Verbal Learning Test improved by 1.04 and 0.83 standard deviations above baseline. Additionally, Complex Figure Test short-term and long-term recall mean scores improved by 1.56 and 1.38 standard deviations above baseline as well.</td>
</tr>
</tbody>
</table>

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

**Discussion**

Zhang et al. (2004) conducted a randomized placebo controlled double-blind cross-over trial of 18 post-acute TBI patients which demonstrated that donepezil significantly increased scores on tasks of sustained attention and short-term memory when compared to placebo and that these improved results were sustained after the wash-
out period. 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 Rey Auditory Verbal Memory Test (RAVMT) showed significant improvement (p<0.05). To assess improvement in executive function, results from the Stroop-colour naming test showed significant changes (p<0.03). On the test for Attentional Performance (TAP) a significant change was noted on the divided attention (errors) subsection of the test.

In a sixteen-week open-label study, mean scores for short-term and long-term recall on the Rey Auditory Verbal Learning Test improved by 1.04 and .83 standard deviations above baseline. Complex Figure Test short-term and long-term recall mean scores improved by 1.56 and 1.38 standard deviations above baseline as well (Masanic et al., 2001). Similar findings were also reported by Morey and colleagues (2003).

**Conclusion**

*Based on a single RCT, there is Level 1b evidence that donepezil improves attention and short-term memory post ABI.*

**Donepezil helps to improve attention and short-term memory following brain injury.**

### 6.4.2 Methylphenidate

Methylphenidate is a stimulant whose exact mechanism is unknown (Napolitano et al., 2005). Although it is thought to act on the presynaptic nerve and it also acts to restrain the reabsorption of serotonin and norepinephrine (Kim et al., 2006). Methylphenidate has been extensively used as a treatment for attention deficit disorder, as well as narcolepsy with both the TBI and non-BTI populations (Glenn 1998).

**Individual Studies**

**Table 6.19 Effect of Methylphenidate on Cognitive Functioning**

<table>
<thead>
<tr>
<th>Author/Year/Country/Study design/PEDro Score</th>
<th>Methods</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kim et al., (2012) USA RCT</td>
<td>N=33 Participants were randomized to either the treatment (Methylphenidate-MPH) group or a control (placebo) group, although only 18 completed the study.</td>
<td>Those in the MPH group showed an improvement in accuracy and reaction time in the sustained attention task, but only reaction time in the working</td>
</tr>
<tr>
<td>Author/Year/Country/Study design/PEDro Score</td>
<td>Methods</td>
<td>Outcome</td>
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<td>--------------------------------------------</td>
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<tr>
<td><strong>PEDro = 7</strong></td>
<td>Those in the treatment group were given a single dose of 0.3mg/kg rounded to the nearest 2.5 mg of methylphenidate on each of the testing days. Each group performed a visual sustained attention task (VAST) along with two back tasks.</td>
<td>memory task. Response time on the two-back task was faster on MPH than on placebo. Accuracy was also greater for those in the MPH group but this difference was not significant.</td>
</tr>
<tr>
<td><strong>Willmott and Ponsford (2009)</strong> RCT PEDro = 10</td>
<td>N=40 Patients received either methylphenidate 0.3mg/kg BID rounded to the nearest 2.5 mg or a placebo. Patients were seen for 6 sessions across 2 week period. Sessions were in 3 blocks, with patients receiving the MHD on one session of each block. Placebo was given on the other session.</td>
<td>MHD was seen to improve the speed of processing information without reducing the accuracy of the information being processed. When looking at the results of the various scales used to measure speed at which information is processed, significant increases were seen on all (the Ruff 2 and 7 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, Rating Scale of Attentional Beh.) while patients were on the MHD. If note individuals with lower GCS also had much slower processing speed. Results of symbol digit modalities test was seen to significantly improve in these patients while on the MHD.</td>
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<tr>
<td><strong>Kim et al., (2006)</strong> Korea RCT PEDro = 6</td>
<td>N=18 Double-blind placebo-controlled trial of subjects with TBI. The participants were randomly divided into one of two treatment groups: (1) single-dose (20mg) of methylphenidate; or (2) placebo. Outcome measured using visuospatial attention tasks.</td>
<td>Improvements in response accuracy were demonstrated in favour of the treatment group although not to a level of statistical significance.</td>
</tr>
<tr>
<td><strong>Plenger et al., (1996)</strong> USA RCT PEDro = 5</td>
<td>N=23 Double-blind RCT of subjects ranging in age from 16 to 64 years administered .30 mg/kg of methylphenidate twice a day. 9 subjects completed the study</td>
<td>Methylphenidate significantly improved attention.</td>
</tr>
<tr>
<td><strong>Whyte et al., (2004)</strong> USA RCT</td>
<td>N=34 Double-blind crossover study of methylphenidate (0.3 mg/kg/dose) versus placebo measured by sustained/divided arousal, attention, distraction tasks with</td>
<td>54 dependent variables reduced to 13 composite factors revealing significance in three treatment effects: information processing speed</td>
</tr>
</tbody>
</table>
Evidence-Based Review of Moderate to Severe Acquired Brain Injury

### Author/Year/Country/Study design/PEDro Score

<table>
<thead>
<tr>
<th>PEDro</th>
<th>Methods</th>
<th>Outcome</th>
</tr>
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<tbody>
<tr>
<td>8</td>
<td>varying target rates on subjects, between 16 and 60 with a non-penetrating TBI resulting in LOC (GCS&lt;12), PTA &gt; 1 hour or a focal abnormality (neuro-imaging); outcome measures included subject response as well as reports from treating clinicians and caregivers.</td>
<td>(p&lt;0.001), work task attentiveness (p=0.01), and caregiver attention ratings (p=0.01). Of 13 independent variables, one showed significant treatment effects: reaction time before errors in sustained attention to response task (p=0.03). No treatment-related improvements observed in susceptibility to distraction, and divided or sustained attention.</td>
</tr>
<tr>
<td>7</td>
<td>N=12 Moderate-to-severe closed-head-injury patients randomly assigned to a treatment group receiving 0.3mg/kg bid of methylphenidate for 1 week followed by placebo, and control group receiving a placebo for 1 week followed by methylphenidate treatment. Attention, cognitive processing speed, learning and social personality functioning measures applied at the end of each week, 1 hr after last dose.</td>
<td>No significant differences found between drug and placebo condition in any outcome measure.</td>
</tr>
<tr>
<td>6</td>
<td>N=6 Individuals who had sustained a TBI were selected to participate in the current study. Participants were administered 5 to 10 mg of MHP over a 2 week period. Medication was gradually reduced at this point. Participants were evaluated before, during and after the administration of MPH.</td>
<td>Prior to treatment, patients were found to have great difficulty in shifting attention between hemifields. Once patients were placed on MHP, an improvement in the asymmetry was noted. This improvement was also noted 2 weeks after the medication was discontinued. Study authors noted that left side recovery improved once the medication was begun. Overall MPH improved attentional imbalance in patients post TBI.</td>
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</table>

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

**Discussion**

Several studies have investigated the effectiveness of methylphenidate on cognitive rehabilitation post ABI. In the most recent Kim et al. (2012) found reaction time and accuracy in the sustained attention task improvement significantly while on the methylphenidate. Willmott and Ponsford (2009) found that administering methylphenidate to a group of patients during inpatient rehabilitation, did significantly improve the speed of information processing. In a RCT examining the effects of
methylphenidate, a psychostimulant on attention, 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. Another RCT by Plenger et al. (1996) also found that methylphenidate significantly improved attention.

Speech et al. (1993) conducted a double blind placebo controlled trial evaluating the effects of the stimulant medication methylphenidate following closed head injury. Here the administration of methylphenidate did not significantly improve attention, information processing speed, or learning compared to placebo on. This is in contrast to the results noted by Whyte et al. (2004) and Plenger et al. (1996). 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, once again results did not reach significance. In the case series conducted by Pavlovskaya et al. (2007), methylphenidate was found to significantly improve the patients’ ability to shift their attention from a precure on the right to one on the left.

Conclusions

Although several of the studies reviewed found methylphenidate did improve cognitive functioning post ABI, the results were conflicting. To date there is no clear evidence supporting the administration of methylphenidate to improve cognitive functioning in individuals who have a moderate to severe ABI.

The effectiveness of methylphenidate treatment to improve cognitive impairment following brain injury is unclear.
6.4.3 Sertraline

Individual Studies

Table 6.20: Effect of Sertraline on Cognitive Functioning Post ABI.

<table>
<thead>
<tr>
<th>Author/Year/Country/Study design/PEDro Scores</th>
<th>Methods</th>
<th>Outcome</th>
</tr>
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<tbody>
<tr>
<td>Banos et al., (2010) USA RCT PEDro = 9</td>
<td>N=99 Individuals with a moderate to severe TBI were recruited within the first 8 weeks post injury. All were randomized to either the treatment group (n=49 - sertraline 50 mg 1xdaily) or placebo (n=50). Patients were assessed at 3, 6 and 12 months. Outcome measures used to assess patients were: Wechsler memory scale, trail making test, Wechsler adult intelligence scale, neurobehavioral functioning inventory.</td>
<td>More subjects in the treatment group were seen to have dropped out at each of the 3 assessment points. Those in the placebo groups at the 6th and 12th month assessment period were older than the control group and had higher GCS. Overall, there were not significant differences between the two groups, thus early administration of sertraline was not found to improve cognitive functioning during the first year post ABI. In both groups 40-50% of study participants dropped out.</td>
</tr>
</tbody>
</table>

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

Discussion

In an effort to improve cognitive function, Banos et al. (2010) randomly assigned a group of 99 TBI patients to either a control group (n=50) or a treatment group (n=49). The treatment group was administered 50 mg of sertraline once daily, while the control group was administered a placebo. Patients were assessed at 3, 6 and 12 months post sertraline administration. Various neuropsychological tests were completed at each time period. Cognitive functioning was not found to improve following the administration of sertraline.

Conclusions

**There is Level 1b evidence showing that sertraline does not improve cognitive functioning in individuals who have sustained a moderate to severe ABI.**

*Sertraline has not been shown to improve cognitive functioning within the first 12 months post injury.*
6.4.4 Amantadine
Amantadine is a non-competitive N-methyl-D-aspartate receptor antagonist and is currently used as an antiviral agent used as a prophylaxis for influenza A, for the treatment of neurological diseases such as Parkinson’s Disease and in the treatment of neuroleptic side-effects such as dystonia, akinthesia and neuroleptic malignant syndrome (Schneider et al., 1999). It is also thought to work pre- and post-synaptically by increasing the amount of dopamine (Napolitano et al., 2005). One study was identified that investigated the effectiveness of amantadine as a treatment for the remediation of learning and memory deficits and cognitive functioning following brain injury.

Individual Studies

<table>
<thead>
<tr>
<th>Author/Year/Country/Study design/PEDro Score</th>
<th>Methods</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Schneider et al., (1999) USA RCT PEDro= 5</td>
<td>N=20 TBI rehabilitation subjects randomly assigned to treatment and placebo groups to test the effectiveness of amantadine on cognitive and behavioural rehabilitation.</td>
<td>Although there was a general trend towards improvement, results did not reach significance when treatment and placebo groups were compared using ANOVA and regression analysis (p=0.732).</td>
</tr>
<tr>
<td>Kraus et al., (2005) USA Pre-Post</td>
<td>N=22 subjects with chronic brain injury and complaints of cognitive impairment participated in this pre- and post- 12-week treatment. Patients were given 400mg of amantadine.</td>
<td>No significant differences were noted on measures of attention or memory deficits.</td>
</tr>
</tbody>
</table>

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

Discussion
In this RCT completed by Schneider et al. (1999) the effects of amantadine on cognition and behaviors was assessed. Here, twenty patients were included in the study and each were prescribed amantadine for 2 weeks. Statistical comparison of results evaluating the five subsets of attention, executive/flexibility, memory, behavior and orientation did not demonstrate any significant effect for the use of amantadine. Kraus et al. (2005) again looked at the effects on executive functioning amantadine has on individuals who have sustained a moderate to severe TBI. Of note no significant differences were found for measures of memory deficits or attention.
Conclusions

There is Level 2 evidence from one RCT that Amantadine does not help to improve overall cognitive functioning based on the conclusions of a single RCT.

There is Level 2 evidence that amantadine does not help to improve learning and memory deficits based on the conclusions of a single group intervention study.

Amantadine may not be an effective treatment to improve learning and memory deficits and executive function following brain injury.

6.4.5 Pramiracetam

Pramiracetam is a nootropic or cognitive activator that facilitates learning and treats memory deficiencies and other cognitive problems. It produces an increased turnover of acetylcholine in hippocampal cholinergic nerve terminals and its at least 100 times more effective than its original compound piracetam (McLean, Jr. et al., 1991).

Individual Studies

Table 6.22 Effect of Pramiracetam on Memory Post ABI

<table>
<thead>
<tr>
<th>Author/Year/Country/Study design/PEDro Score</th>
<th>Methods</th>
<th>Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>McLean Jr. et al., (1991) USA RCT PEDro=7</td>
<td>N=4 Double-blind RCT of a small group of males aged 24-37 treated with two 3-week blocks each of 400 mg of oral pramiracetam TID and placebo over 12 weeks.</td>
<td>Clinically significant improvements were found for memory after the administration of pramiracetam. These improvements remained at one month after discontinuation of the drug.</td>
</tr>
</tbody>
</table>

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

Discussion

McLean Jr. et al. (1991) conducted a double-blind, placebo-controlled, randomized trial on pramiracetam on 4 males aged 24-37. The medication was given orally to the subjects in a 400 mg dose three times per day and its effects on memory and cognition were assessed. Clinically significant improvements were found for memory and these improvements remained at one month following discontinuation of the drug.
Conclusions

Based on a single RCT, there is Level 1b evidence that pramiracetam produces significant clinical improvements on males’ memory which is sustained at one month following discontinuation of the drug.

Pramiracetam may improve memory in males.

6.4.6 Physostigmine
Physostigmine is a cholinergic agonist that temporarily stops acetylcholinesterase, which in turn slows the destruction and increases the concentration of acetylcholine at the synapse. Its use in Alzheimer’s disease has been examined at length. It has also been proposed to improve memory in head-injured patients (McLean, Jr. et al., 1987).

Individual Studies

Table 6.23 Effect of Physostigmine on Memory Post ABI

<table>
<thead>
<tr>
<th>Author/Year Country/Study design/PEDro Score</th>
<th>Methods</th>
<th>Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardenas et al., (1994) USA RCT PEDro=6</td>
<td>N=36 Double blind RCT of men with brain injury who were randomized to receive physostigmine, scopolamine, and placebo.</td>
<td>44% of the participants experienced improved memory scores with the use of physostigmine.</td>
</tr>
</tbody>
</table>

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

Discussion
Cardenas et al. (1994) conducted a double-blind, placebo-controlled study on 36 men with brain injury who were randomized to receive either oral physostigmine, scopolamine, or placebo. Improved memory scores were found for 44% of the subjects who received oral physostigmine with the Long-term Storage section of the Selective Reminding Test being the most sensitive measure of this.

Conclusions

Based on a single RCT, there is Level 1b evidence that physostigmine improves memory in men with brain injury.
6.4.7 Bromocriptine
Bromocriptine is a dopaminergic agonist, which primarily affects D\textsubscript{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 seen in motor abilities. Four studies have been identified investigating the use of bromocriptine as an adequate treatment for the recovery of cognitive impairments following brain injury.

**Individual Study**

<table>
<thead>
<tr>
<th>Author/Year/Country/Study design/PEDro Score</th>
<th>Methods</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Whyte et al., (2008) USA RCT PEDro=7</td>
<td>N=12 Bromocriptine or placebo was administered for 4 weeks, (starting dose was 1.25 mg/BID, final dose was 5 mg/BID). Medication was increased every 2 days until the dose reached 5 mg BID. During week 4 the medication was tapered until it was eliminated. Once this phase was complete the group was put on the placebo. The placebo group then became the bromocriptine group. Study continued for about 8 weeks. During the study participants engaged in various attention tasks: Sustained arousal and attention task (50/50), sustained arousal and attention task (20/80), speed/accuracy trade off task, distraction task, choice RT task, dual task, sustained attention to response to task, test of everyday attention, inattentive behaviour task, classroom attentiveness, attention ratings.</td>
<td>It was noted that several participants did experience moderate to severe drug effects and withdrew or were withdrawn from the study. Test results for all subjects indicate bromocriptine had little significant effect on their abilities to perform on a range of measures of attentional function.</td>
</tr>
<tr>
<td>McDowell et al., (1998) USA RCT PEDro = 4</td>
<td>N=24 Subjects suffering a TBI (closed or open) with loss of consciousness (GCS &lt; 8). Patients randomized into treatment (Bromocriptine 2.5 mg) and placebo groups. Measures required prefrontal</td>
<td>Central executive testing: following drug treatment there were significant improvements on dual task counting (p=0.028), dual task digit span (p=0.016), trail making test (p=0.013), Stroop</td>
</tr>
<tr>
<td>Author/Year/Country/Study design/PEDro Score</td>
<td>Methods</td>
<td>Outcome</td>
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<tr>
<td>Powell et al., (1996) UK Case series</td>
<td>cortex function (working memory, executive control) and were administered using a laptop computer (except trail making and control task) Testing took place 90 minutes after pill administration.</td>
<td>Interference Test (p=0.05), FAS Test (p=0.02), Wisconsin Card Sorting (p=0.041). The treatment drug had no significant effects on working memory tasks (p=0.978), or control tests (p=0.095)</td>
</tr>
</tbody>
</table>

**Discussion**

Bromocriptine is a dopaminergic agonist, which is believed to have an effect on frontal lobe functioning. In a randomized placebo controlled cross over study Whyte et al. (2008) administered bromocriptine to a group of individuals. Administration of bromocriptine was begun with a dose of 1.25mg/BID and increased to 5mg/BID. Individuals received the medication for 3 weeks before being titrated off the medication and placed on a placebo. Test results for all subjects indicate bromocriptine had little significant effect on their abilities to perform on a range of measures of attentional function. It was noted that several participants did experience moderate to severe drug effects and withdrew or were withdrawn from the study. In an earlier study, McDowell et al. (1998) examined the effects of low dose bromocriptine in a double-blinded, placebo-controlled cross-over design trial. Testing revealed that a low dose of bromocriptine (2.5 mg/daily) improved functioning on tests of executive control including a dual task, trailmaking test, the Stroop test, the Wisconsin Card-Sorting Test and the controlled oral word association test (FAS test). However, bromocriptine did not significantly influence working memory tasks.

Powell et al. (1996) carried out a multiple baseline design on eleven patients with TBI or subarachnoid haemorrhage who were administered bromocriptine. Motivational deficits were the main outcomes measured and they were quantified using innovative structured tools that could measure anxiety and depression for instance. Improvements were found on all measures assessed except mood.

Although the McDowell et al. (1998) study demonstrated benefits following administration of bromocriptine, there was only a single administration of
bromocriptine or placebo 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 (2.5mg 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**

*Based on a two RCTs there is conflicting evidence supporting the use of bromocriptine to enhance cognitive functioning.*

*There is Level 4 evidence that bromocriptine improves all motivational deficits except mood.*

*There is Level 5 evidence, from one observational study, that bromocriptine significantly improves memory impairments.*

**Bromocriptine improves some executive cognitive functions such as dual-task performance and motivational deficits, but it does not consistently improve memory. More research is needed before the benefits of using bromocriptine to enhance cognitive functioning are known.**

### 6.4.8 Cerebrolysin

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.” Cerebrolysin has been demonstrated to have neuroprotective and neurotrophic effects, and has been linked to increased cognitive performance in an elderly population.
Individual Studies

Table 6.25 Effect of Cerebrolysin on Cognitive Functioning Following Brain Injury

<table>
<thead>
<tr>
<th>Author/Year/Country/Study design</th>
<th>Methods</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alvarez et al., (2003) Spain Pre-Post</td>
<td><strong>N=20</strong> Post-acute TBI subjects (etiology not specified, severity determined by initial GCS score) received 20 – 30 ml I.V. Injections of Cerebrolysin solution over 4 weeks. Research staff measured brain bioelectrical activity, cognitive performance and clinical outcome.</td>
<td>Significant decrease in slow brain bioelectrical activity (delta: p &lt; 0.01; theta: p &lt; 0.05); significantly enhanced relative beta activity power (p &lt; 0.01). EEG power ratio scores significantly reduced (p &lt; 0.01) after treatment. Patients with a multi-point evaluation of EEG/brain mapping activity, power ratio scores decreased significantly after treatment (p &lt; 0.05) compared with baseline. Significant improvement in Syndrom-Kurztest (SKT) cognitive performance test scores after treatment (p &lt; 0.01). Patients with a multi-point cognitive evaluation, SKT scores decreased significantly compared to baseline after treatment (p &lt;0.05), but not 3 months later. Significant improvement in GOS scores after treatment (p &lt; 0.05). Significant decrease in serum urea levels and body temperature after treatment (p &lt; 0.05).</td>
</tr>
</tbody>
</table>

Discussion

In an open label trial of 20 brain-injured patients, Alvarez et al. (2003) investigated the potential benefits of using cerebrolysin which was administered intravenously 20 times over a 4-week period. Although the study included patients with mild, moderate or severe traumatic brain injury based on the Glasgow Coma Scale score, all patients had significant disability ranging from moderate disability to persistent vegetative state on the Glasgow Outcome Scale. The time since injury varied from 23 to 1107 days with 9 cases less than 1 year post injury and 11 cases greater than 1 year post injury. A brief neuro-psychological battery (SKT) using 9 tests to specifically evaluate memory and attention demonstrated overall significant improvement for the 9 of 20 patients for whom it could be administered. Glasgow Outcome Scores also significantly improved comparing pre to post intervention scores.

Conclusions

*There is Level 4 evidence that cerebrolysin, a neurotrophic and neuroprotective medication appears to have potential benefit to improve outcome and cognitive*
functioning post-brain injury; however, controlled trials will be necessary to evaluate this further.

Cerebrolysin may be beneficial for the improvement of cognitive functioning following brain injury.

6.4.9 Growth Hormone (GH) Replacement Therapy and Cognitive Rehabilitation Post ABI
Following an ABI, it is not uncommon for individuals to be diagnosed with hypopituitarism. In fact as many as 25 to 40 % of individuals with a moderate to severe ABI have demonstrated chronic hypopituitarism (Kelly et al. 2006; Schneiderman et al., 2008; Bondanelli et al., 2007). Despite this few patients are screened for Growth Hormone Deficiencies (GHD), thus the link between cognitive impairment and GHD has not yet been definitively established (High, Jr. et al., 2010). There is very little literature available on the benefits of GH replacement therapy after a TBI.

Individual Studies

Table 6.26 rh(GH) and its Impact on Cognitive Functioning Post ABI

<table>
<thead>
<tr>
<th>Author/Year/Country/Study design/PEDro Scores</th>
<th>Methods</th>
<th>Outcome</th>
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</table>
| High Jr et al., (2010) USA PEDro = 8        | N=23 Those in the treatment group (n=12) were given rhGH. Initially the drug was administered at 200 ug, followed by a 200 ug increase every month until the dosage reached 600 ug. IGF-1 levels were then tested. The control group (n=11) was given a placebo. Both groups received these injections (placebo or rhGH) for one year. During the time patients were given a variety of neuro-psychological tests to assess language, visual/spatial functioning, upper extremity motor functioning, information processing efficiency, working memory/attention, learning and memory, executive, intellectual and emotional functioning. | Overall study results did not show great improvements on the majority of neuropsychological tests between the two groups. There was however improvement on 4 of the tests used: (1) Finger tapping demonstrated a significant improvement between the treatment and the control group (p<0.01). (2) Processing Speed Index: the treatment group improved significantly over the one year period (p<0.05) and although the control group showed improvement at the end of the first 6 months (p<0.01) this was not seen at the end of the first year. Significant improvement was also noted on the (3) Wisconsin Card Sorting Test (executive functioning) for the treatment group. (4) On the
<table>
<thead>
<tr>
<th>Study</th>
<th>Country</th>
<th>Design</th>
<th>N</th>
<th>Participants</th>
<th>Results</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Silver et al., (2006) USA RCT PEDro=9</td>
<td>N=123 Participants were randomly assigned to receive either rivastigmine 3 to 6 mg per day or placebo. Both the medication and the placebo were administered with food. At the end of the first 4 weeks, rivastigmine doses were increased to 3.0 mg BID provided the patient did not experience any adverse events. If necessary doses were decreased to 1.5 mg BID or 4.5 mg BID (3mg in the am and 1.5 in the mg). Principle assessment tools were the Trails A and B, Hopkins verbal learning test (HVLT) and the Cambridge neuropsychological test automated battery rapid visual information processing (CANTAB RVIP) A’. Results of the CANTAB RVIP A’ and HVLT found no significant differences between the placebo group and the treatment group. Overall, rivastigmine was found to be well tolerated and safe.</td>
<td>California Verbal learning Test-II improvement was noted for the treatment group on learning and memory.</td>
<td>Silver et al., (2006) USA RCT PEDro=9</td>
<td>N=123 Participants were randomly assigned to receive either rivastigmine 3 to 6 mg per day or placebo. Both the medication and the placebo were administered with food. At the end of the first 4 weeks, rivastigmine doses were increased to 3.0 mg BID provided the patient did not experience any adverse events. If necessary doses were decreased to 1.5 mg BID or 4.5 mg BID (3mg in the am and 1.5 in the mg). Principle assessment tools were the Trails A and B, Hopkins verbal learning test (HVLT) and the Cambridge neuropsychological test automated battery rapid visual information processing (CANTAB RVIP) A’. Results of the CANTAB RVIP A’ and HVLT found no significant differences between the placebo group and the treatment group. Overall, rivastigmine was found to be well tolerated and safe.</td>
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<tr>
<td>Silver et al., (2009) USA Cohort</td>
<td>N=98 Individuals who had participated in the 2006 study (see above) were asked to participate in the 2009 study. All were started on rivastigmine 1.5mg BID and slowly this was increased to a maximum of 12mg/day. Dose increased occurred only if the patient was stable on the previous dose for 4 weeks. The mean final dose of rivastigmine was 7.9mg/day. At the end of the study period all (n=98) were seen to improve of the CANTAB RVIP A’ (p&lt;0.001), the HVLT (P&lt;0.001), and the Trails A and B (p&lt;0.001). Further analysis of the subgroup of individuals who were diagnosed with moderate to severe memory impairment, the group was seen to improve significantly on all measures.</td>
<td></td>
<td>Silver et al., (2009) USA Cohort</td>
<td>N=98 Individuals who had participated in the 2006 study (see above) were asked to participate in the 2009 study. All were started on rivastigmine 1.5mg BID and slowly this was increased to a maximum of 12mg/day. Dose increased occurred only if the patient was stable on the previous dose for 4 weeks. The mean final dose of rivastigmine was 7.9mg/day. At the end of the study period all (n=98) were seen to improve of the CANTAB RVIP A’ (p&lt;0.001), the HVLT (P&lt;0.001), and the Trails A and B (p&lt;0.001). Further analysis of the subgroup of individuals who were diagnosed with moderate to severe memory impairment, the group was seen to improve significantly on all measures.</td>
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<tr>
<td>Reimunde et al., (2011) Spain Cohort</td>
<td>N=19 Patients (only males involved with the study) in the treatment group (n=11) were administered recombinant human GH (rhGH), subcutaneously, .5mg/day for 20 days, then 1 mg/day for 5days each week. The control group (n=8) was given a placebo (1mg/day 5/days/week). All patients were also involved with an individualized cognitive program. Individuals receiving the GH treatment were found to have significant improvement in their IGF-I plasma levels following 3 months of treatment (p&lt;0.01). These values were similar the control group. Results of the WAIS indicated that the control group improved significantly on the digits and manipulative intelligence quotient (p&lt;0.05). For those in the treatment groups improvement was noted on: understanding digits, numbers and incomplete figures (p&lt;0.05) and similarities vocabulary, verbal IQ, Manipulative IQ, and total IQ (p&lt;0.01).</td>
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<td>Reimunde et al., (2011) Spain Cohort</td>
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PEDro = Physiotherapy Evidence Database rating scale score (Moseley et al. 2002).
Discussion
In two RCTs rivastigmine was administered to patients who had sustained a moderate to severe TBI (Silver et al., 2006; Silver et al., 2009). Study results, from both studies, indicate that rivastigmine did improve cognitive function and memory impairment, although results were not significant. In Silver’s (2009) follow-up open-label cohort study at the end of 38 week study period participants (n=98) did show significant improvement on the CANTAB RVIP A’, the HVLT and the trail A and B scales; however when comparing the results of the two groups, those in the ex-rivastigmine group to those in the ex-placebo group, the improvements were not significant.

Reimunde et al. (2011) in a cohort study looking at the benefits of administering rhGH to a group of patients who have sustained either a moderate or severe TBI for a three month period. 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) and 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 suggesting rhGH does assist in improving cognitive functioning in individuals who are GHD post ABI.

There is Level 2 evidence showing the administration of rhGH does improve cognitive rehabilitation in those who have sustained a moderate to severe TBI.

The administration of rhGH results in improved cognitive performance in patients who been diagnosed has having a growth hormone deficiency post ABI. Due to the small sample sizes of both studies, further research with larger samples is recommended.
6.5 Conclusions

1. There is Level 2 evidence to suggest that specific structured training programs designed to improve attention are ineffective or at best equivocal in their effects on attention.

2. There is Level 2 evidence that dual task training has a positive effect on divided attention.

3. There is Level 2 evidence that dual-task training on is effective on the speed of processing.

4. There is Level 3 evidence that individuals with a TBI perform poorly on dual task activities due to their inability to maintain a measure of sustained attention.

5. There is Level 3 evidence that reaction times of those with a TBI are slower than the reaction times of those without.

6. There is Level 1a evidence supporting the use of active or high tech external aids (assistive technology) as a compensatory strategy for memory impairments.

7. There is Level 2 evidence supporting the use of passive or no tech/low tech aids in improving memory impairments post ABI.

8. There is conflicting evidence supporting the use of computer assisted cognitive retraining as an adjunct to the rehabilitation program, especially regarding attentional retraining following brain injury. Although some improvement in memory was found in a few of the studies it was not found in all. General cognitive functioning did appear to benefit from computer assisted cognitive retraining; however, further study confirming these findings need to be conducted.

9. There is Level 2 evidence of a positive impact on visual and verbal learning post exercise intervention for brain injury survivors.

10. There is Level 3 evidence from one study indicating that VR programs do not enhance cognitive functioning post TBI in individuals who have sustained a TBI.

11. There is Level 2 evidence (from several studies) that internal strategies appear to be an effective aid in improving recall performance.
12. There is Level 3 evidence from several case-control studies that internal strategies appear to assist in improving recall performance.

13. There is Level 2 evidence indicating that memory-retraining programs appear effective, particularly for functional recovery although performance on specific tests of memory may or may not change.

14. There is Level 3 evidence supporting spaced retrieval practice as an effective method of improving memory post ABI.

15. There is Level 3 evidence suggesting that the spacing of repetitions improves memory post ABI.

16. There is Level 1b evidence, from one RCT, that cranial electrotherapy stimulation did not help to improve memory and recall following brain injury.

17. There is conflicting evidence supporting the use of group-based interventions to treat executive dysfunction post ABI.

18. There is Level 2 evidence to suggest that goals training is effective in improving attention and executive control.

19. There is Level 2 evidence, based on a single RCT, that goal management training is effective for improving paper and pencil everyday tasks and meal preparation skills for persons with an ABI.

20. There is Level 4 evidence, based on a single group intervention, that goal planning in the form of leisure activities is effective for achieving identified goals following injury.

21. There is conflicting evidence as to the effectiveness of cognitive rehabilitation programs focusing on memory strategies and selective attention.

22. There is Level 2 evidence that general cognitive rehabilitation therapy post acquired brain injury is effective for improving cognition. Although there are variable strategies and protocols for cognitive rehabilitation, all comprehensive interventions appear to provide benefit.

23. There is Level 4 evidence that working memory training is effective in recovering the central executive system of working memory.
24. There is Level 4 evidence that an outpatient day program is effective for assisting brain injury survivors in returning to competitive employment.

25. Based on a single RCT, there is Level 1b evidence that donepezil improves attention and short-term memory.

26. Although several of the studies reviewed found methylphenidate did improve cognitive functioning post ABI, the results were conflicting. To date there is no clear evidence supporting the administration of methylphenidate in individuals who have a moderate to severe ABI.

27. There is Level 1b evidence showing that sertraline does not improve cognitive functioning in individuals who have sustained a moderate to severe ABI.

28. There is Level 2 evidence that amantadine does not help to improve learning and memory deficits based on the conclusions of a single group intervention study.

29. There is Level 2 evidence from one RCT that amantadine does not help to improve overall cognitive functioning based on the conclusions of a single RCT.

30. Based on a single RCT, there is Level 1b evidence that pramiracetam produces significant clinical improvements on males’ memory which is sustained at one month following discontinuation of the drug.

31. Based on a single RCT, there is Level 1b evidence that physostigmine improves memory in men with brain injury.

32. Based on a two RCTs there is conflicting evidence supporting the use of bromocriptine to enhance cognitive functioning.

33. There is Level 4 evidence that bromocriptine improves all motivational deficits except mood.

34. There is Level 5 evidence, from one observational study, that bromocriptine significantly improves memory impairments.

35. There is Level 4 evidence that cerebrolysin, a neurotrophic and neuroprotective medication appears to have potential benefit to improve outcome and cognitive functioning post-brain injury; however, controlled trials will be necessary to evaluate this further.
36. There is Level 1b evidence suggesting rhGH does assist in improving cognitive functioning in individuals who are GHD post ABI.

37. There is Level 2 evidence showing the administration of rhGH does improve cognitive rehabilitation in those who have sustained a moderate to severe TBI.
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