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EFNS TASK FORCE/CME ARTICLE

EFNS guidelines on cognitive rehabilitation: report of an EFNS task force

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Disorders of language, spatial perception, attention, memory, calculation and praxis are a frequent consequence of acquired brain damage [in particular, stroke and traumatic brain injury (TBI)] and a major determinant of disability. The rehabilitation of aphasia and, more recently, of other cognitive disorders is an important area of neurological rehabilitation. We report here a review of the available evidence about effectiveness of cognitive rehabilitation. Given the limited number and generally low quality of randomized clinical trials (RCTs) in this area of therapeutic intervention, the Task Force considered, besides the available Cochrane reviews, evidence of lower classes which was critically analysed until a consensus was reached. In particular, we considered evidence from small group or single cases studies including an appropriate statistical evaluation of effect sizes. The general conclusion is that there is evidence to award a grade A, B or C recommendation to some forms of cognitive rehabilitation in patients with neuropsychological deficits in the post-acute stage after a focal brain lesion (stroke, TBI). These include aphasia therapy, rehabilitation of unilateral spatial neglect (ULN), attentional training in the post-acute stage after TBI, the use of electronic memory aids in memory disorders, and the treatment of apraxia with compensatory strategies. There is clearly a need for adequately designed studies in this area, which should take into account specific problems such as patient heterogeneity and treatment standardization.

Objectives

The rehabilitation of disorders of cognitive functions (language, spatial perception, attention, memory, calculation, praxis), following acquired neurological damage of different aetiology [in particular, stroke and traumatic brain injury (TBI)], is an expanding area of neurological rehabilitation, and has been the focus of considerable research interest in recent years. In 1999 a Task Force on Cognitive Rehabilitation was set up under the auspices of the European Federation of Neurological Societies. The aim was to evaluate the existing evidence for the clinical effectiveness of cognitive rehabilitation in stroke and TBI, and provide recommendations for neurological practice. The present guidelines are an update and a revision of the previous work, which was published in 2003 in the *European Journal of Neurology* (Cappa *et al.*, 2003).

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Background

For these guidelines, we have limited ourselves to a review of studies dealing with the rehabilitation of non-progressive neuropsychological disorders due to stroke and traumatic brain damage (TBI). As a consequence several important areas of 'cognitive rehabilitation' were excluded such as the rehabilitation of dementia, psychiatric and developmental disorders. In addition, we have not considered pharmacological treatment and rehabilitation.

The prevalence and relevance of cognitive rehabilitation for stroke and TBI patients requires to establish recommendations for the practice of cognitive rehabilitation, and has been formally recognized by a subcommittee of the Brain Injury-Interdisciplinary Special Interest Group of the American Congress of Rehabilitation Medicine. The initial recommendations of the Committee were published in 1992 as the Guidelines for Cognitive Rehabilitation (Harley *et al.*, 1992) and were based on the so-called 'expert opinion', which did not take into account empirical evidence on the effectiveness of cognitive rehabilitation. More recently, a review of the scientific literature for cognitive rehabilitation in TBI patients published from

January 1988 through August 1998 (including 11 randomized clinical trials – RCTs) noted that data on the effectiveness of cognitive rehabilitation programmes were limited by the heterogeneity of subjects, interventions, and outcomes studied (NIH Consensus Development Panel, 1999).

As a preliminary consideration, we wish to underline that the present status of studies on the effectiveness of cognitive rehabilitation is unsatisfactory. We are fully convinced that the standards required for the evaluation of pharmacological and surgical interventions also apply to rehabilitation. In particular, it is necessary to show that rehabilitation is effective not only in modifying the impairment but also in by having sustained effects at the disability level. Unfortunately, the majority of RCTs in this area are of poor methodological quality, have insufficient sample size and/or fail to assess the outcome at the disability level. Many other studies fail to compare intervention with placebo or sham treatment.

Search strategy

Each member of the Task Force was assigned an area of cognitive rehabilitation (SFC-aphasia; SC-unilateral neglect; BR-attention; BS-memory; CvH-apraxia; TB-acalculia) and systematically searched the EBM Reviews – Cochrane Central Register of Controlled Trials, the Medline and PsychInfo databases using the appropriate key words, and searched textbooks and existing guidelines. The general consensus was to include articles only if they contained data which could be rated according to the grades of recommendation for management, classified in terms of level of evidence following the guidance statement for neurological management guidelines of the European Federation of Neurological Societies-revised (Brainin *et al.*, 2004).

Method for reaching consensus

Data collection and analysis of evidence was performed independently by each participant according to the assignment mentioned above. On the basis of the single reports, SFC produced a first draft of the guidelines. These were circulated several times amongst the Task Force members until the discrepancies on each topic were solved, and a consensus was reached.

Results

Rehabilitation of aphasia

The rehabilitation of speech and language disorders following brain damage is the area of intervention for acquired cognitive deficits with the longest tradition, dating back to the 19th century (Howard and Hatfield, 1987). A variety of approaches have been applied to the rehabilitation of aphasia, from stimulation approaches to the recent attempts to establish theory-driven treatment programmes based on the principles of cognitive neuropsychology (Basso *et al.*, 2003). The need to establish the effectiveness of aphasia rehabilitation has stimulated a number of investigations, dating back to the period after the Second World War, and has been based on a variety of methodologies. A meta-analysis of studies dealing with the effectiveness of language rehabilitation, limited to aphasia as a result of stroke, has been made available by the Cochrane collaboration. The review covers articles about speech and language rehabilitation after stroke up to January 1999 (Greener *et al.*, 2000). The conclusion of the review is that 'speech and language therapy treatment for people with aphasia after a stroke has not been shown either to be clearly effective or clearly ineffective within an RCT. Decisions about the management of patients must therefore be based on other forms of evidence. Further research is required to find out if speech and language therapy for aphasic patients is effective. If researchers choose to do a trial, this must be large enough to have adequate statistical power, and be clearly reported.' This conclusion is based on a limited number of RCTs (12), all of which were considered of poor quality. Another review by Cicerone *et al.* (2000) reached a different conclusion. The conclusion is that 'cognitive-linguistic therapies' can be considered as Practice Standard for aphasia after stroke; similar, positive conclusions for TBI were based on less consistent evidence. The reasons for this discrepancy can be found in the different criteria used in the two reviews. Several studies included by Cicerone *et al.* (2000) were not considered in the Cochrane review for the following reasons. In comparison with an untreated control group, one study by Hagen (1973) was excluded because of the lack of true randomization (the patients were sequentially assigned to treatment or no treatment). Another study (Katz and Wertz, 1997) was probably excluded because it dealt only with computer-assisted reading rehabilitation. Two small RCTs (Helffenstein and Wechsler, 1982; Thomas-Stonell *et al.*, 1994), which reported positive treatment effects, were excluded from the Cochrane review because they were devoted to communication disorders after TBI.

Some of the RCT comparing therapy with unstructured stimulation were based on a very limited number of treatment sessions. A meta-analysis by Bhogal *et al.* (2003) showed that studies reporting a significant treatment effect provided 8.8 h of therapy per week for 11.2 weeks, whilst the negative studies only provided approximately 2 h per week for 22.9 weeks. Total length of therapy was significantly inversely correlated with mean change in Porch Index of Communicative Abilities (PICA) scores. The number of hours of therapy provided in a week was significantly correlated to greater improvement on the PICA and the token test. These results suggest that an intense therapy programme provided over a short amount of time can improve outcomes of speech and language therapy for stroke patients with aphasia.

The Cochrane review does not include class II and class III evidence. Thus, it excluded the three large studies by Basso *et al.* (1979); Shewan and Kertesz (1985) and Poeck *et al.* (1989), all indicating significant benefits of treatment. An additional small class II study by Carlomagno *et al.* (2001) supported the usefulness of writing rehabilitation in patients in the post-acute stage. Additional evidence for treatment effects comes from some recent randomized investigations on small patient samples (class II). A study comparing group communication treatment with 'deferred treatment' indicated positive effects on both linguistic and communication measures (Elman and Bernstein-Ellis, 1999). Another study based on a small sample compared 'massed' with conventional treatment and showed a significant superiority of the 'massed' intervention (Pulvermueller *et al.*, 2000). A recent randomized study compared semantic with phonological treatment of anomia. Both treatments resulted in a significant improvement in functional communication (Doesborgh *et al.*, 2004).

Similarly, single case studies are not considered in the Cochrane reviews. This is particularly relevant because most of the recent treatment studies based on the cognitive neuropsychological approach make use of the single case methodology. A review paper by Robey *et al.* (1999) critically discusses this approach and concludes that generally a large treatment effect has been found in aphasic patients.

Recommendation

The conclusions of the Cochrane review of aphasia rehabilitation after stroke are not compatible with grade A recommendation for aphasia therapy. There is however considerable evidence from class II and III studies, as well as from rigorous single-case studies indicating its probable effectiveness (grade B recommendation). There is clearly a need for further investigations in the field. In particular, the evidence of effectiveness of pragmatic-conversational therapy after TBI is based on a limited number of studies on small samples and is in need of confirmation.

Rehabilitation of unilateral spatial neglect

The presence of hemineglect beyond the acute stage is associated with poor outcome in terms of independence (Denes *et al.*, 1982; Stone *et al.*, 1992) and considerable effort is therefore devoted to its rehabilitation. We review here published studies of neglect rehabilitation, and refer also to recently published reviews (Robertson, 1999; Robertson and Hawkins, 1999; Diamond, 2001; Pierce and Buxbaum, 2002; Kerkhoff, 2003; Paton *et al.*, 2004), including the Cochrane review (Bowen *et al.*, 2002). The latter analysed 15 studies and found evidence that cognitive rehabilitation resulted in significant and persisting improvements in performance on impairment level assessments. There was, however, insufficient evidence to confirm or exclude an effect of cognitive rehabilitation at the level of disability or on destination following discharge from hospital. Different types of approaches are currently used for neglect rehabilitation; we review here evidence for these different approaches.

Combined training of visual scanning, reading, copying and figure description yielded statistically significant improvement of neglect symptoms in one class II (Antonucci *et al.*, 1995) and two class III studies (Pizzamiglio *et al.*, 1992; Vallar *et al.*, 1997). Visual scanning training alone was shown to improve significantly neglect in one class I study (Weinberg *et al.*, 1977). *Spatiomotor or visuo-spatiomotor cueing* improved neglect significantly in one class I (Kalra *et al.*, 1997) and two class III studies (Lin *et al.*, 1996; Frassinetti *et al.*, 2001). *Visual cueing with kinetic stimuli* was found to bring significant, albeit transient, improvement in three class III studies (Butter *et al.*, 1990; Pizzamiglio *et al.*, 1990; Butter and Kirsch, 1995). However, the use of optokinetic stimulation did not improve neglect in a recent class I study (Pizzamiglio *et al.*, 2004). *Video feedback* (Tham and Tegnér, 1997) and *visuomotor feedback* (Harvey *et al.*, 2003) were shown to improve significantly performance on trained tasks in class III and II studies respectively. *Training of sustained attention*, *increasing of alertness or cueing of spatial attention* were shown to improve significantly neglect in class III studies (Hommel *et al.*, 1990; Ladavas *et al.*, 1994; Robertson *et al.*, 1995; Kerkhoff, 1998).

Several studies investigated effects of *influencing multisensory representations*. These studies in general demonstrated transient effects, lasting little longer than the end of the appropriate stimulation. Vestibular stimulation by cold-water infusion into the left outer ear canal showed significant effects on different aspects of the unilateral neglect in two class III studies (Rode and Perenin, 1994; Rode *et al.*, 1998). Galvanic vestibular stimulation improved significantly neglect symptoms in one class III study (Rorsman *et al.*, 1999). Transcutaneous electrical stimulation of the left neck muscles showed significant effects in three class III studies (Vallar *et al.*, 1995; Guariglia *et al.*, 1998; Perennou *et al.*, 2001) and neck muscle vibration in one class II study (Schindler *et al.*, 2002). The latter is the only study of this group showing a persistent effect after 2 months. Changes in trunk orientation had significantly positive effects in one class II study (Wiart *et al.*, 1997).

The use of *prism goggles* deviating by 10 degrees to the right, introduced relatively recently, was shown to improve significantly, in a transient fashion, neglect symptoms in two class II (Rossetti *et al.*, 1998; Angeli *et al.*, 2004) and one class III study (Farne *et al.*, 2002). A class III study applied the prism goggle treatment for a 2-week period and obtained statistically significant improvement in long-term (Frassinetti *et al.*, 2002). *Forced use of left visual hemifield or left eye* showed a relative benefit in neglect in one class II (Beis *et al.*, 1999) and two class III studies (Butter and Kirsch, 1992; Walker *et al.*, 1996).

Computer training yielded mixed results. One class I (Robertson *et al.*, 1990) and one class III study (Bergego *et al.*, 1997) reported absence of significantly positive effects, whilst a more recent class II study showed statistically significant improvement in wheel chair mobility (Webster *et al.*, 2001).

Recommendation

Several methods of neglect rehabilitation were investigated in level I or II studies. The present evidence confers level A recommendation to visual scanning training and to visuo-spatio-motor training, and level B recommendation to the combined training of visual scanning, reading, copying and figure description; to trunk orientation; to neck vibration; and to forced use of left eye. The use of prism goggles obtains the same level of recommendation for transient effect and level C for long-term effect if used over longer periods. Level B recommendation exists for video feedback; and level B–C for training of sustained attention and alertness. Level C of recommendation is valid for transient effects because of caloric or galvanic vestibular stimulations as well as transcutaneous electrical stimulation of neck muscles. Visual cueing with kinetic stimuli and the use of computers in neglect rehabilitation remain controversial.

Rehabilitation of attention disorders

Attention deficits follow many types of brain damage, including stroke and TBI (Bruhn and Parsons, 1971; Van Zomeren and Van DenBurg, 1985). A pioneer study by Ben-Yishay *et al.* (1978) explored the treatment of deficits in focusing and sustaining attention in 40 brain-injured adults. There was not only improvement on the attention training tasks, but also generalization to other psychometric measures of attention which were maintained at 6-month follow-up. Using a multiple-baseline design, with patients at 4–6 years after head injury, Wood (1986) found that contingent token reinforcement was effective in increasing patients' ability to sustain attention on a task. Several studies (Ponsford and Kinsella, 1988; Niemann *et al.*, 1990; Novack *et al.*, 1996) have explicitly incorporated and/or evaluated therapeutic interventions such as feedback, reinforcement and strategy teaching into the attention rehabilitation programmes.

The Cochrane review by Lincoln *et al.* (2000), having searched for controlled trials of attention training in stroke, identified only the study of Schoettke (1997) showing the efficacy of the attention training in improving sustained attention.

Thirteen studies were reviewed by Cicerone *et al.* (2000), including three prospective RCTs (Niemann *et al.*, 1990; Gray *et al.*, 1992; Novack *et al.*, 1996), four class II controlled studies (Strache, 1987; Ponsford and Kinsella, 1988; Sohlberg and Mateer, 1989; Sturm and Wilmes, 1991); and six class III studies (Wood, 1986; Ethier *et al.*, 1989; Gray and Robertson, 1989; Gansler and McCaffrey, 1991; Wilson and Robertson, 1992; Sturm *et al.*, 1997). Most controlled studies compared attention training with an alternative treatment, without including a no-treatment condition; a very important distinction is between studies conducted in the acute and post-acute stage. Cicerone *et al.* (2000) concluded that evidence from two RCT (Niemann *et al.*, 1990; Gray *et al.*, 1992) with a total of 57 subjects and two controlled studies (Strache, 1987; Sohlberg and Mateer, 1989) with a total of 49 subjects supports the effectiveness of attention training beyond the effects of non-specific cognitive stimulation for subjects with TBI or stroke during the post-acute phase of recovery and rehabilitation. Cicerone *et al.* (2000) recommended such a form of intervention as a practice guideline for these persons. Interventions should include not only training with different stimulus modalities and complexity, but also therapist activities such as monitoring subjects' performance, providing feedback and teaching strategies. Attention training appears to be more effective when directed at improving the subject's performance on more complex, functional tasks. However, the effects of treatment may be relatively small or task-specific, and an additional need exists to examine the impact of attention treatment on activities of daily living (ADL) or functional outcomes.

Acute studies

One class I and two class II studies evaluated the effectiveness of attention treatment during the acute period of rehabilitation. The class I study of Novack *et al.* (1996) compared the effectiveness of focused treatment consisting of sequential, hierarchical interventions directed at specific attention mechanisms versus unstructured intervention consisting of non-sequential, non-hierarchical activities requiring memory or reasoning skills. Both groups improved, but there were no intergroup differences: the observed improvements are probably because of spontaneous recovery. One class II study (Ponsford and Kinsella, 1988) used a multiple baseline design across subjects and evaluated a programme for the remediation of processing speed deficits in 10 patients with severe TBI (6–34 weeks post-injury). The authors reported no benefit or generalization of effects of attention training: however, improvement did occur in some patients when practice on attention training tasks was combined with therapist feedback and praise. In the other class II study (Sturm and Wilmes, 1991), 35 subjects with lateralized stroke showed beneficial effects of attention training on 5 of 14 outcome measures, especially on measures of perceptual speed and selective attention in left hemisphere lesions.

Post-acute

Two class I and two class II studies assessed the attention treatment effectiveness during the post-acute period of rehabilitation. Gray *et al.* (1992) treated 31 patients with attention dysfunction, randomly assigned to receive either computerized attention retraining or an equivalent amount of recreational computer use. Immediately after training, the experimental group showed marked improvement on two measures of attention (but, when pre-morbid intelligence score and time since injury were added as covariates, the treatment effect was no longer significant); at 6-month follow-up, the treatment group showed continued improvement and superior performance in respect with the control group on tests involving auditory–verbal working memory. The authors suggested that the improvement, continuing over the follow-up period, was consistent with a strategy training model as it becomes increasingly automated and integrated into a wider range of behaviours (Gray *et al.*, 1992). In the second post-acute class I study (Niemann *et al.*, 1990) community-dwelling patients with moderate to severe brain injury were screened for orientation, vision, aphasia and psychiatric illness. The experimental attention training group improved significantly more than the alternative (memory) treatment group on four attention measures administered throughout the treatment period, although the effects did not generalize to the second set of neuropsychological measures. Sohlberg and Mateer (1989) employed a class II multiple baseline design with four patients to evaluate the effectiveness of a specific, hierarchical attention training programme. All subjects showed gain on a single attention outcome measure administered after the start of attention training but not after training on visuospatial processing: this improvement also generalized to cognitive and everyday problems. Strache (1987) conducted a prospective class II study on patients with mixed trauma and vascular aetiologies, and compared two closely related interventions for concentration with subjects in an untreated control group receiving general rehabilitation. After 20 treatment sessions, both attention treatments resulted in significant improvement on attention measures in respect of control subjects, with some generalization to memory and intelligence measures. Rath *et al.* (2004) in three inter-related class II controlled studies examined the construct of problem solving as it relates to the assessment of deficits in higher level outpatients with TBD. The difference between the groups were significant first for timed attention tasks, then for psychosocial and problem solving self-report inventories, then for patients self-report problem solving and also in self-report inventory. It means that it is necessary to have a lot of different approaches to the construct of problem solving (multidimensional approach) to obtain a good rehabilitation. Several attempts were made to establish the differential role for effectiveness of training of specific components of attention. Rios *et al.* (2004) in a class II controlled study on TBI consider attention as a basic cognitive function, a prerequisite for other cognitive processes. It is divided into four different subprocesses: cognitive flexibility, speed of processing, interference and working memory, which must be taken into consideration. The results of the work support the view that these different subprocesses of attentional control can be differentiated between high and low level processes and may have implications for neuropsychological assessment and rehabilitation.

Improvements in speed of processing appear to be less robust than improvements on non-speeded tasks (Ponsford and Kinsella, 1988; Ethier *et al.*, 1989; Sturm *et al.*, 1997). Moreover, several studies also suggest greater benefits of attention training on more complex tasks requiring selective or divided attention than on basic tasks of reaction time or vigilance (Sturm and Wilmes, 1991; Gray *et al.*, 1992; Sturm *et al.*, 1997). Wilson and Robertson (1992), implementing a series of individualized interventions intended to facilitate voluntary control over attention during functional activities, effectively decreased the attention lapses that the subject experienced when reading novels and texts.

Recommendation

During the acute period of recovery and inpatient rehabilitation, evidence is insufficient to distinguish the effects of specific attention training from spontaneous recovery or more general cognitive interventions for patients with moderate-to-severe TBI and stroke. Therefore, specific interventions for attention during the period of acute recovery are not recommended. On the contrary, the availability of class I evidence for attention training in the post-acute phase after TBI is compatible with a grade A recommendation.

Rehabilitation of memory

Memory impairment is a well documented sequel following TBI and has also been reported following stroke. Some studies investigating memory rehabilitation are oriented towards alleviating general memory problems such as problems of learning and retrieval or everyday functioning problems. Others focus on specific contents such as orientation, dates, names, faces, routines and appointments. Again others are oriented towards modality specific impairments such as visual versus verbal memory problems. As memory is not a unitary concept, studies also address different aspects of memory such as working memory or prospective memory.

The studies reviewed roughly fall into three categories: studies targeting techniques without external memory aids, studies targeting techniques with non-electronic external memory aids, and studies focusing on the use of assistive electronic technologies [for a review of the application of external memory aids and computer-based procedures for the enhancement of memory functioning in neurological patients with memory deficits see Kapur *et al.*, 2004)].

Studies targeting techniques without external memory aids

The effectiveness of training memory strategies without external aids in memory rehabilitation was investigated by three class III studies. Doornhein and de Haan (1998) (class III) investigated memory impairment in 12 stroke patients. Memory strategy training was performed with the target group for 4 weeks at two sessions per week. The training programme consisted of six memory strategies for the target group and non-specific training involving repetitive practice on memory tasks for the control group. At the end of the treatment, a significant difference between the groups on a test of face-name associations was found. However, the weighted mean difference showed that memory strategy training had no significant effects on memory impairment or subjective memory complaints. Berg *et al.* (1991) (class III study) investigated memory strategy training versus drill and repetitive practice versus no treatment in 39 TBI patients. Only the strategy-training group showed improved memory functions and the largest effect was observed 4 months after therapy. Ryan and Ruff (1988) (class III study) investigated 20 TBI patients using rehearsal and visual imagery strategies on association and chaining tasks versus some alternative treatment. After 6 weeks of training both groups showed improved memory functioning. The training was most beneficial for subjects with mild memory impairment before treatment.

In summary, one class III study did not find positive effects on memory impairment using compensatory strategies, whereas another class III study reported positive effects and yet another class III only found a training effect for mild memory impairment.

Several class III studies have compared errorless learning (people were prevented from making errors) and errorful learning (such as trial-and-error) in people with memory impairments and shown that the participants (stroke and TBI patients with mixed aetiologies) benefited most when learning without errors was encouraged (Baddeley and Wilson, 1994; Squires *et al.*, 1997; Hunkin *et al.*, 1998). A quantitative meta-analysis on implicit learning and memory rehabilitation in TBI, stroke and Alzheimer's patients was performed by Kessels and de Haan (2003) (class IV study). The authors compared the errorless learning and vanishing cues methods. The authors found an advantage of errorless learning techniques over trial-and-error learning. They also observed that the superiority of a learning technique such as errorless learning may depend on the exact task used and the way in which memory is tested. This is exemplified by Riley *et al.* (2004) (class III) who compared the efficacy of errorless learning without fading (ELWF) and the method of vanishing cues (MVC) asking whether MVC or ELWF produced better implicit or explicit memory performance. MVC led to better performance than ELWF when effortful but successful study-trial recall was elicited suggesting a positive effect of MVC on explicit memory. With respect to implicit memory, MCV was more effective than ELWF when a stem completion task was used but not when a free association task or perceptual identification task was used. The authors concluded that the relative effectiveness of the two methods depended on the way in which memory was tested. In another class III study researchers compared errorless learning and errorful learning with or without pre-exposing the participants (TBI and stroke patients) to the target stimuli (Kalla *et al.*, 2001). The authors reported a significant advantage for errorless learning compared with errorful learning. Pre-exposure of the target stimuli strongly enhanced the advantage of errorless learning. In a multi-center study, Wilson *et al.* (2001) performed nine experiments in three study phases comparing 'errorless' and 'trial-and-error (errorful)' learning in patients with different aetiologies including stroke and TBI patients. The authors found that preventing memory impaired patients from making errors (errorless learning) in situations which facilitated retrieval of implicit memory for the learned material (but not in situations which required the explicit recall of novel associations) had a positive effect on learning. Their results also suggested that under certain circumstances errorless learning might be more beneficial for more severely memory-impaired patients.

In summary, a series of class III studies reports an advantage of errorless learning techniques over errorful techniques. There is some indication that any benefit of errorless learning may depend on the type of task used, the way in which memory is tested and on the severity of the memory impairment. Pre-exposition to the target stimuli seems to enhance the benefit or errorless learning.

A different learning technique was investigated by Hillary *et al.* (2003) (class III study). The authors investigated whether learning in moderate to severe TBI is improved by learning a spacing-of-repetitions procedure using consecutive learning trials as a control condition. The spacing-of-repetitions procedure is based on the spacing effect which has been shown to improve learning and memory when repeated trials are distributed over time (spaced repetitions). The authors found that the participants recalled and recognized significantly more spaced words than massed words during the word list-learning task. Statistically accounting for the different neuropsychological status of the patients, there remained a significant influence of the spacing effect on recall and recognition performance. These results support findings of an earlier class III study (Schacter *et al.*, 1985) in which the spaced retrieval technique was investigated in four mild to severely memory-impaired patients. Better performance for learning new information was reported.

In summary, Two class III studies report an advantageous effect of spaced retrieval techniques on specific memory performance.

Studies targeting techniques with non-electronic external memory aids

External aids such as keeping a notebook or a diary has been investigated by two class III studies and a series of single case studies (class IV studies). Schmitter-Edgecombe *et al.* (1995) (class III study) investigated notebook training treatment in TBI patients and reported significantly fewer everyday memory failures in the notebook group compared with a support treatment group. Ownsworth and McFarland (1999) (class III) investigated the efficacy of a diary only (DO) training versus a diary plus self-instructional training (DSIT) approach in patients with different aetiologies including TBI and stroke patients. When compared with the DO group, the DSIT group maintained a more consistent use of the diary strategy over time, reported a lower level of memory difficulties and rated the strategies used as more helpful.

In summary, Two class III studies support the use of external non-electronic memory aids such as a notebook or diary. It seems that a combined treatment of an external memory aid (diary) and internal strategy training increases efficacy.

The effectiveness of external non-electronic memory aids has also been shown by several case studies or uncontrolled studies (class IV studies; Sohlberg and Mateer, 1989; Zencius *et al.*, 1990; Burke *et al.*, 1994; Squires *et al.*, 1996). There is one class IV study that seems to suggest that not all aids or strategies are beneficial. Evans *et al.* (2003) investigated the use of memory aids or strategies in a large number of participants with brain damage with different aetiologies. The most commonly used memory aids were external aids such as calendars, lists, notebooks, and diaries. However, from the efficacy ratings obtained from the relatives/independent persons the most widely used aids/strategies were not necessarily considered to be the most effective.

The use of assistive electronic technologies

The increasing availability of computers, the internet, wireless connections, and other electronic devices opens a wide range of possibilities to incorporate these technologies into memory rehabilitation [for a review on assistive technology for cognition (ATC) devices see LoPresti *et al.*, 2004)]. It is surprising that despite the relatively low costs and increasing availability there are still relatively few well controlled studies. An early class III study by Kerner and Acker (1985) (class III study) showed improved memory performance of mild to moderately memory impaired TBI patients after using computer-based memory training software. Support for the efficacy of computer-assisted memory training also comes from some class IV studies (Glisky and Glisky, 2002; Kapur *et al.*, 2004). Another class III study tested the effectiveness of four different computer-assisted memory-training strategies (self pacing, feedback, personalized, visual presentation) in closed-head injury Chinese patients (Tam and Man, 2004). Comparing the pre-test and post-test memory outcome (computer quiz scores) of the patient and study group showed significant improvement for all four memory tasks but not in an independent memory outcome measure. Besides computers, portable paging systems have been used to enhance memory performance. Wilson *et al.* (2001) (class III) investigated the effectiveness of a portable externally programmed paging system (NeuroPage) in a large number of TBI, stroke, and other patients with memory and/or planning/organizational problems. More than 80% of the patients who completed the 16 week trial showed a significant improvement in carrying out everyday activities (such as self care, self medication, keeping appointments) when using the pager system, and this improvement was maintained when they were evaluated 7 weeks after returning the pager. It is noteworthy to mention that this research has been extended by Inglis *et al.* (2002) who developed an interactive memory aid using PDA's with data transmission via the mobile phone network. Neuropage can thus also communicate with the carer's computer system who can thus remotely monitor the use and functionality of the PDA. No controlled efficacy study has been published yet. Successful use of an alphanumeric paging system has also been shown in a class IV TBI single case study (Kirsch *et al.*, 2004). Another electronic memory aid device is the portable voice organizer (VO). This device can be trained to recognize a patient's individual speech patterns, store messages dictated by the user and replay messages at pre-specified time-periods. Hart *et al.* (2002) investigated the efficacy of such a system in memory impaired TBI patients aimed at facilitating the recall of therapy goals and plans in a controlled within-subject design (class III study). Results showed that recorded goals were recalled significantly better than unrecorded goals in both free and cued recall conditions. The authors point out that caution needs to be applied to generalizing the results because of the low number of subjects, the short training time and the lack of independent memory measures. The efficacy of the VO has also been demonstrated in a well-controlled class IV study with patients of different aetiologies including TBI patients (van den Broek *et al.*, 2000). Virtual reality technology has been used in memory assessment to provide more ecologically valid and controlled evaluation than is possible in rehabilitation settings. Its usefulness in memory rehabilitation has been investigated in two class III studies (for a review of the use and possibilities of virtual reality in memory rehabilitation see Brooks and Rose, 2003). Two class III studies investigated the performance of patients when specific memory tasks were performed in a virtual environment. The effect of active and passive participation in a non-immersive virtual environment on spatial memory in stroke patients was investigated Rose *et al.* (1999) (class III study). The participants' performance in spatial and object recognition memory tests was evaluated after active exploration of the virtual environment or passive observation of the spatial layout of the virtual environment. The stroke patients as well as the controls showed better performance in the active than in the passive spatial recognition task. However, whereas passive controls performed better on the object recognition task than active controls, the patients did not show any difference on the active versus passive object recognition task. Grealy *et al.* (1999) (class III) investigated the impact of non-immersive virtual stimulating exercise environments on attention, information processing, learning and memory in TBI patients. A comparison of the pre- and post-intervention scores showed significant improvements on the tests of attention, information processing, verbal and visual learning. No improvement was found on memory functions tested by the logical memory test and the complex figure test.

The two class III studies indicate that patients can improve on spatial memory performance or verbal and visual learning in a virtual environment.

Recommendations

Cicerone *et al.* (2000) (using a different rating system from the one used here) recommended compensatory memory training for subjects with mild memory impairments as a practice standard. These authors point out that independence in daily function, active involvement in identifying the memory problem to be treated and the capability and motivation to continue active and independent strategy use strongly contribute to effective memory remediation. Based on the currently available evidence we judge the use of memory strategies without electronic aid as possibly effective (level C) although it remains unclear to what degree the benefit depends on the severity of the memory impairment. Specific learning strategies such as errorless learning are supported by a series of class III studies and are thus rated as probably effective (level B). However, some studies suggest that the efficacy of a specific learning technique may depend on the task used, whether implicit or explicit memory is implicated, and the severity of the memory impairment. Two class III studies supported by several class IV studies have shown possible efficacy (level C recommendation) of non-electronic external memory aids such as diary or notebook keeping. Electronic external memory devices such as computers, paging systems or portable voice organizers have been shown to be effective in several class III studies and are thus recommended as probably effective (level B) aids for improving TBI or stroke patients' everyday activities. The use of virtual environments has shown positive effects on verbal, visual and spatial learning in stroke and TBI patient in two class III studies. A direct comparison of performing learning and memory training in virtual environments versus non-virtual environments is still lacking and no recommendation can be made as to the specificity of the technique. Currently, memory training in virtual environments is rated as possibly effective (level C).

Despite the many studies investigating memory rehabilitation, the problems raised in previous reports concerning the heterogeneity of the population studied (in terms of age, aetiology and type of brain damage, severity of brain-damage, severity of functional impairments, time post-onset) and the subsequent difficulty of interpreting the results are still valid. It is conceivable that the type and intensity of training has different effects depending on the neural circuits damaged, the functional impairment profile, the age and gender of the patient, the time post-injury, the education level of the patient, and other external factors (such as social and vocational situation). The number of variables involved makes generalization across individuals difficult and favours training programmes tailored to the individual circumstances. No specific recommendations are made for different diagnostic groups or stages of severity. There is still a lack of studies that directly compare patients with different aetiologies (e.g. stroke versus TBI), type and severity of brain damage, age, gender, or stage of recovery.

Rehabilitation of apraxia

Although the incidence of apraxia after acquired brain damage is considerable, the literature on recovery and treatment is very minimal. Several reasons for this lack of evidence can be identified (Maher and Ochipa, 1997). First, patients with apraxia often seem to be unaware of their deficit and rarely complain; secondly, many researchers believe that recovery from apraxia is spontaneous and treatment is not necessary; thirdly, some authors believe that apraxia only occurs when performance is requested of patients in testing situations, and that correct behaviour is displayed in natural settings. By now, however, there is agreement that apraxia hinders ADL independence. Goldenberg *et al.* (2001) assessed complex ADL in patients with apraxia and controls. They found that apraxic patients had more difficulties than patients with left brain damage without apraxia and healthy controls. In two other studies comparable results were found: Hanna-Paddy *et al.* (2003) found a significant relationship between apraxia severity and dependency in physical functioning. Walker *et al.* (2004) studied the impact of cognitive impairments on upper body dressing difficulties after stroke using video analysis; those patients who failed shirt dressing showed neglect and apraxia at follow up. These results suggest that treatment of apraxia should be part of the overall neurorehabilitation programme after brain damage. In this brief summary, studies examining the effectiveness of treating apraxia will be reviewed. The studies are labelled either observational or experimental and the quality of the studies is described.

There are two recent RCTs on the rehabilitation of apraxia. Smania *et al.* (2000) assessed in an RCT the effectiveness of a rehabilitative training programme for patients with limb apraxia. Thirteen patients with acquired brain injury and limb apraxia (lasting more than 2 months) as a result of lesions in the left cerebral hemisphere participated in the study. The study group underwent an experimental training for limb apraxia consisting of a behavioural training programme with gesture-production exercises. The control group received conventional treatment for aphasia. Assessments involved neuropsychological tests of aphasia, verbal comprehension, general intelligence, oral apraxia, constructional apraxia and three tests concerning limb praxic function (ideational and ideomotor apraxia and gesture recognition). Everyday activities related to each test were used to measure the outcome. The patients in the study group achieved a significant improvement of performance in both ideational and ideomotor apraxia tests. They also showed a significant reduction of errors in ideational and ideomotor apraxia tests. The change in performance was not significant for the control group. The results show the possible effectiveness of a specific training programme for the treatment of limb apraxia. Donkervoort *et al.* (2002) determined in a controlled study the efficacy of strategy training in left hemisphere stroke patients with apraxia. A total of 113 left hemisphere stroke patients with apraxia were randomly assigned to two treatment groups: (i) strategy training integrated into usual occupational therapy and (ii) usual occupational therapy only. The primary outcome measure was a standardized ADL observation by a blinded research assistant. Additional ADL measures were used as secondary outcome measures (Barthel ADL index, ADL judgement by occupational therapists and by patients). After 8 weeks of treatment, patients who received strategy training ($n = 43$) improved significantly more than patients in the usual treatment group ($n = 39$) on the ADL observations. This reflects a small-to-medium effect (effect size 0.37) of strategy training on ADL functioning. With respect to the secondary outcome measures a medium effect (effect size 0.47) was found on the Barthel ADL index. No beneficial effects of strategy training were found after 5 months (at follow-up).

Recently we performed secondary analyses on the data of Donkervoort *et al.* (2002) to examine the transfer of the effects of cognitive strategy training for stroke patients with apraxia from trained to non-trained tasks. The analyses showed that in both treatment groups, the scores on the ADL observations for non-trained tasks improved significantly after 8 weeks of training as compared with the baseline score. Change scores of non-trained activities were larger in the strategy-training group as compared with the usual treatment group. These results suggest that transfer of training is possible, although further research should confirm these exploratory findings (Geusgens *et al.*, 2005).

Several class II studies also support the efficacy of apraxia rehabilitation. Goldenberg and Hagman (1998) studied a group of 15 patients with apraxia, who made fatal errors in ADL: an error was rated as fatal if the patient could not proceed without help or if the error prohibited the patient from accomplishing the task successfully. The study design was as follows: each week an ADL test was performed; between tests one of three activities was trained, whereas support, but no therapeutic advice, was given for two other activities. Each week another activity was trained, whilst the other activities were performed in daily life. The next week another activity was trained and in the third week the remaining activity. In case fatal errors were still seen during performance, another cycle of therapy was run. At the end of therapy, 10 patients could perform all three activities without fatal errors. Three patients made only one fatal error. No generalization of training effects was found from trained to non-trained activities. Seven patients were re-examined after 6 months: only those patients who kept practising the activities in their daily life, still showed the positive results of the training.

Van Heugten *et al.* (1998) performed a study evaluating a therapy programme for teaching patients strategies to compensate for the presence of apraxia. The outcome was studied in a pre–post-test design; measurements were conducted at baseline and after 12 weeks of therapy. Thirty-three stroke patients with apraxia were treated at occupational therapy departments in general hospitals, rehabilitation centres and nursing homes. The patients showed large improvements in ADL functioning on all measures and small improvements on the apraxia test and motor functioning test. The effect sizes for the disabilities, ranging from 0.92 to 1.06, were large compared with the effect sizes for apraxia (0.34) and motor functioning (0.19). The significant effect of treatment is also seen when individual improvement and subjective improvement are considered. These results suggest that the programme seems to be successful in teaching patients compensatory strategies that enable them to function more independently, despite the lasting presence of apraxia. Poole (1998) published a study examining the ability of participants with left-hemisphere stroke to learn one-handed shoe tying. Participants with left hemisphere stroke with and without apraxia and control participants were taught how to tie their shoes with one hand. Retention was assessed after a 5-min interval during which participants performed other tasks. All groups differed significantly in regard to the number of trials to learn the task. However, on the retention task, the control adults and the stroke patients without apraxia required similar numbers of trials whilst the participants with apraxia required significantly more trials than the other two groups. All groups required fewer trials on the retention task than on the learning task.

Further evidence is provided by single case studies. Wilson (1988) studied a female adolescent with extensive damage to the brain following an anaesthetic accident. One of the most disabling consequences of the damage was apraxia, which made her almost completely dependent in daily life. Wilson concluded that the step-by-step programme was successful in teaching the patient some tasks, but generalization to new tasks was not found at follow-up. Maher *et al.* (1991) studied the effects of treatment on a 55-year-old man with ideomotor apraxia and preserved gesture recognition. Daily 1-h therapy sessions were given during a 2-week period. During therapy sessions many cues were offered which were withdrawn systematically whilst feedback and correction of errors were given as well. The production of gestures improved qualitatively. Ochipa *et al.* (1995) subsequently developed a treatment programme aimed at specific error types. Praxis performance was studied in two stroke patients. It appeared that both patients achieved considerable improvement in performance but the observed effects were treatment specific: treatment of a specific error type did not improve across untreated gestures. Jantra *et al.* (1992) studied a 61-year-old man with a right-sided stroke followed by apraxic gait. After 3 weeks of gait training supplemented with visual cues, the patient became independent with safe ambulating. Pilgrim and Humphreys (1994) presented a case of a left-handed head injured patient with ideomotor apraxia of his left upper limb. The patient's performance on the 10 objects was measured before and after training in three different modalities. A mixed design analysis of variance (ANOVA) was carried out showing a positive effect of therapy, but little carry-over to everyday life. Bulter (1997) presents a case study which explores the effectiveness of tactile and kinaesthetic stimulation as an intervention strategy, in addition to visual and verbal mediation, in the rehabilitation of a man with ideational and ideomotor apraxia following a head injury. The results indicated some improvement after a training period and limited evidence of the effectiveness of additional sensory input.

Goldenberg *et al.* (2001) conducted a therapy study with six apraxic patients in which two methods of treatment were compared: direct training of the activity based on the guided performance of the whole activity and exploration training aimed at teaching the patient structure-function relationships underlying correct performance but which did not involve actual completion of the activity. Exploration training had no effect on performance, whereas direct training of the activity reduced errors and need for assistance. Training effects were largely preserved at follow up, but the rate of errors increased when the trained activities were tested with a partially different set of objects. Performance improved with repeated testing of untrained activities during initial baseline, but there was no reduction of errors or amount of assistance required for untrained activities during training of other activities. As therapeutic results were restricted to trained activities and to some degree to trained objects, the authors conclude that therapy should be tailored to the specific needs of the patients and their family and should be tied closely to the normal routines of daily life.

Recommendation

There is grade A evidence for the effectiveness of apraxia treatment with compensatory strategies. Treatment should focus on functional activities, which are structured and practised using errorless learning approaches. As transfer of training is difficult to achieve, training should focus on specific activities in a specific context close to the normal routines of the patients. Recovery of apraxia should not be the goal for rehabilitation. Further studies of treatment interventions are needed, which also address if the treatment effects generalize to non-trained activities and situations.

Rehabilitation of acalculia

Disorders of number processing and calculation (DNPC) may occur after many types of brain damage. Depending on the underlying disease and on lesion location, the frequency of calculation disorders in patients with neurological disorders has been estimated to range between 10% and 90% (Jackson and Warrington, 1986).

Two main types of rationales have been applied to DNPC. One, the 'reconstitution' or 're-teaching' approach consists of extensive lost or damaged abilities by way of extensive practice. The other, indirect approach promotes the use of 'back-up' strategies based on the patient's residual resources (Girelli *et al.*, 2002). In this case, the treatment would not merely point to restore the functionality of the impaired component but rather to exploit the preserved abilities to compensate for the deficit. Both types of remediation employ step-by-step training consisting in presentation of problems of increasing difficulty, facilitation cues and other types of assistance which are eventually faded with progressive recovery; in all cases direct feedback is provided to the patient on his/her accuracy and errors.

Outcome measures typically consist in comparison of individual's pre- and post-treatment performance in transcoding tasks, simple and complex calculation. Most research designs and statistical evaluation procedures are taken from the field of single-subject research (Kratochwill and Levin, 1992; Randall *et al.*, 1999). The amount of functional disability on daily life is rarely assessed or estimated in this corpus of studies.

As literature search based on data banks resulted unsatisfactory, the authors have reviewed the existing literature themselves and they have used a pre-existing overview related to the topic (Girelli and Seron, 2001).

Studies are mostly 'quasi-experimental' using a single-case or small-group approach guided by the principles of cognitive neuropsychology (Shallice, 1979; Caramazza, 1989; Riddoch and Humphreys, 1994; Seron, 1997) and single-subject research (Kratochwill and Levin, 1992; Randall *et al.*, 1999) (class II, III and IV evidence). Group studies using control groups are considered inadequate by most authors due to known reasons (problems with patient selection, group homogeneity, and heterogeneity of subjacent deficit and premorbid functional level). The recent group study of Gauggel and Billino (2002) deals with the effects of motivation rather than of specific treatment.

Rehabilitation of DNPC may be grouped into several areas of intervention. Rehabilitation of *transcoding ability* (the ability to translate numerical stimuli between different formats) has been successfully performed in several studies (Deloche *et al.*, 1989; Deloche *et al.*, 1989, 1992; Jacquemin *et al.*, 1991; Sullivan *et al.*, 1996), mostly by re-teaching the patient the required set of rules. Impairments of *arithmetical facts* (simple multiplication, addition, subtraction or division solved directly from memory) were the target of several rehabilitation studies (Miceli and Capasso, 1991; Hittmair-Delazer *et al.*, 1994; Girelli and Delazer, 1996; Whestone, 1998; Girelli *et al.*, 2002; Domahs *et al.*, 2003, 2004). In all studies, extensive practice with the defective domain of knowledge, i.e. multiplication tables determined significant improvement. A positive outcome was also reached by a rehabilitation programme based on the strategic use of the patient's residual knowledge of arithmetic (Girelli *et al.*, 2002). This specific case suggests that the integration of declarative, procedural, and conceptual knowledge critically mediates the re-acquisition process. Miceli and

Capasso (1991) have successfully rehabilitated a patient with deficient *arithmetical procedures* (the knowledge required to solve multi-digit calculations). Deficient *arithmetical problem solving* (the ability to provide a solution for complex, multi-step arithmetical text problems) has also been treated in one study (Delazer *et al*., 1998). The study was rated as partly successful by the authors, as patients benefited from the cueing procedure engaged and generated a higher number of correct solution steps, but did not show a prominent effect on the actual execution process.

Recommendation

Overall, the available evidence suggests that rehabilitation procedures used to treat selected variants of DNPC were successful (level C rating). Notably, significant improvements were observed even in severely impaired and chronic patients. Several caveats need to be mentioned in this context. At present, little is known about the prognosis and spontaneous recovery of DNPC, thus, the effects of different interventions in the early stages of numerical disorders may be difficult to evaluate. Moreover, different underlying neurological disorders (e.g. stroke, dementia, and trauma) have only partly been compared as to their specific effects on DNPC. Furthermore, it has not been studied in detail how impairments of attention or executive functions influence the rehabilitation process of DNPC.

General recommendations

In our opinion, there is enough overall evidence to award a grade A, B or C recommendation to some forms of cognitive rehabilitation in patients with neuropsychological deficits in the post-acute stage after a focal brain lesion (stroke, TBI). This general conclusion is based on a limited number of RCTs, and is supported by a considerable amount of evidence coming from class II, III and IV studies. In particular, the use of a rigorous single-case methodology has been considered by the present reviewers as a source of acceptable evidence in this specific field, in which the application of the RCT methodology is difficult for a number of reasons, related to the lack of consensus on the target of treatment, the methodology of the intervention and the assessment of the outcomes.

Future developments

There is clearly a need for large-scale RCTs, evaluating well-defined methodologies of intervention in common clinical conditions (for example, the assessment of the efficacy of an intervention for unilateral spatial neglect (ULN) after RH stroke on long-term motor disability). The main difficulty of this approach lies in the highly heterogeneous nature of cognitive deficits. For example, it is hard to believe that the same standardized aphasia treatment may be effective for a patient with a fluent neologistic jargon and another with agrammatic non-fluent production. Research in neuropsychology has focused on the assessment of specific, theoretically driven treatments on well-defined area of impairment, usually by means of single-case methodology (for example, the effect of a linguistically driven intervention compared with simple stimulation on the ability to retrieve lexical items belonging to a defined class). To the present panel, both approaches represent potentially fruitful avenues for research in this field.

Future studies should also aim at a better clinical and pathological definition of the patients included in the trials. The gross distinction between stroke and TBD used in the present review is clearly insufficient: a separation amongst the main categories of cerebrovascular pathology, and the subdivision on pathological grounds of survivors of TBD can be expected to improve the quality of rehabilitation studies.

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