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Selective and integrated rehabilitation programs for disturbances of visual/spatial attention and executive function after brain damage: a neuropsychological evidence-based review

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The present evidence-based review systematically examines the literature on the neuropsychological rehabilitation of attentional and executive dysfunctions in patients with acquired brain lesions. Four areas are considered: 1) neuropsychological rehabilitation of attentional disorders; 2) neuropsychological rehabilitation of neglect disorders; 3) neuropsychological rehabilitation of dysexecutive disorders and 4) rehabilitation trainings for patients with mild traumatic brain injury (TBI). In each area, search and selection of papers were performed on several databases and integrated by crosschecking references from relevant and recent reviews. The literature up to 2007 was examined (in some areas the search was limited from 2000 to 2007). Class of evidence for each selected study was evaluated according to the SPREAD (2010) criteria. Based on this analysis, recommendations on the effectiveness of rehabilitation trainings are proposed separately for each rehabilitation method in each of the four areas considered. Information on follow-up data and impact on activities of daily living is provided whenever available.

KEY WORDS: Rehabilitation - Neuropsychology - Evidence-based medicine - Executive function - Brain injuries.

Attentional and dysexecutive disturbances are sequelae of brain lesions that have important consequences on the relational life of patients and on their job recovery. In recent years, there has been an increase in experimental studies on these disturbances. This has allowed gathering a considerable amount of evidence on the effectiveness of established rehabilitation programs and has led to the development of new ones.

The aim of the present review was to systematically examine this literature by adopting the evidence-based medicine approach. We referred to the SPREAD [1] criteria and examined the literature prior to 2007 (in some areas the search was limited to 2000-2007; see below). We focused on evaluating the effectiveness of rehabilitation programs for visual-spatial attentional disturbances and executive dysfunctions in patients with brain lesions (rehabilitation treatments for behavioral and psychosocial disorders are presented in a separate report).[2]

Four main areas of research will be considered. First, we will review studies on the recovery of atten-

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tional deficits following specific rehabilitation training. These studies have either focussed on trainings aimed to re-establish specific attentional functions or to foster strategic changes in patients' behavior. Second, a large body of literature has dealt with spatial attention (neglect) deficits. Notably, several new approaches have been tested in recent years, including prism adaptation, transcutaneous electrical stimulation and opto-kinetic stimulation. Third, studies on rehabilitation programs for dysexecutive disturbances will be examined. In these three areas of investigation, studies on acquired brain lesions of different aetiology will be considered, but those on demented patients (with degenerative, multi-infarctual disturbances, etc.) will be excluded. Fourth, in this review we were particularly interested in examining studies on patients with mild traumatic brain injury (TBI). The prognosis of these patients is particularly difficult because of the variability of the sequelae they present. Several studies have proposed integrated rehabilitation programs to deal with attentional and dysexecutive disturbances in these patients.

Neuropsychological rehabilitation of attentional disorders

Attentional disorders are often observed after acquired brain lesions [3], particularly after TBI but also as a consequence of stroke.[4] They can heavily hamper patients' common daily living activities and return to work.[5]

Rehabilitation of attentional disorders was started in the Seventies by Ben-Yishai's team.[6] The authors developed several training tasks, similar to those used for diagnostic purposes, covering the different facets of attentional processes, both intensive (alertness and sustained attention) and selective (selective and divided attention). The general rehabilitative plan was that "drill and practice" on the different tasks, administered with progressively narrower time constraints, could help to remediate patients' difficulties. This "direct" approach has been frequently adopted in subsequent studies too.

A first systematic evidence-based evaluation of rehabilitation of attentional disorders has been published by Cicerone *et al.*,[7] and then recently updated.[8] Another systematic review has been published and subsequently updated by Cappa *et al.*[9, 10] Both studies reached similar conclusions. In particular, Cicerone *et al.*[7] maintained that a specific training for attentional disorders has proven to be effective, and has to be considered as a Practice Guideline in postacute stages after a brain injury, whereas its efficacy in the acute stages is not supported by strong empirical evidence (possible spontaneous recovery). Rehabilitative trainings using complex tasks (strategic tasks) seem to be more successful than training addressed at basic attentional skills. Such conclusion is also shared by Cappa *et al.*[9, 10] In their subsequent update, Cicerone *et al.*[8] further underscored that the best intervention techniques for attentional disorders are those aimed at compensating the cognitive defects ("strategy training") rather than those aimed at rehabilitating the cognitive impairment ("restitution training"). By contrast, quite different conclusions are drawn by Lincoln, Majid and Weyman,[11] who claimed that, in this domain, only two rehabilitation studies satisfy criteria for randomized controlled clinical trials, and concluded that available empirical evidence is not sufficient to support or deny usefulness of rehabilitation of attentional disorders.

Methods

The present review focused on rehabilitation of attentional disorders in patients with acquired, non-degenerative brain lesions. Search and selection of papers were performed on PubMed and PsychINFO databases, integrated by cross-checking references from relevant and recent reviews on the issue.[8, 10, 12]

Papers from the databases were selected if they contained in their title, abstract or key-words the following terms: [(brain OR stroke OR traumatic) AND (attention OR executive) AND (rehabilitation OR treatment OR remediation OR training OR therapy OR intervention)]. In view of the presence of various systematic reviews,[8, 10, 12] search was restricted to experimental studies, reviews and meta-analyses published in English from 2000 to 2007. In this search (as well as in those in the other three targeted areas of investigation) only studies on adult individuals (>18 years) were considered.

The first-run search identified 704 papers, but the direct reading of the title or the abstract allowed excluding articles not relevant for the present aim. The complete reading of the remaining 70 papers allowed us to further exclude studies not concerned with brain-injured patients, non-experimental papers, those not reporting quantitative data, those in

TABLE I.—*Neuropsychological rehabilitation of attentional disorders*

Level of evidence	N papers	N patients (experimental+controls)	Effectiveness	Follow-up	Level of recommendation
		Interventions based on attentional batteries			
APT (Individual)					
1+	1	14+14	±	No	
3	2	5	±	1 out of 2 studies (+)	
APT (Individual) with cognitive-behavioural psychotherapy					
1+	1	20+9	±	No	
APT (Individual) with compensatory strategies					
2–	1	10	±	±	
AIXTENT (Individual)					
2+	1	33	±	No	
3	1	4+4	±	No	
		Interventions based on specific tasks			
Dual task (Individual)					A
2+	1	19+19	±	±	
Endogenous task-shifting (Individual)					
2+	1	18+28	±	±	
		Working memory (Individual)			
1+	1	9+9	+	No	
2+	2	13+4	+(1 out of 2)	No	
		Interventions based on strategies			
1+	1	12+10	±	+	
		Meta-analysis			
1++	1	359	±		
		Review			
2++	1	155	±		

which patients only received pharmacological treatment or occupational therapy, and those specifically focused on return to work.

Results

The final database included 12 papers published from 2000 to 2007, plus 3 papers derived from the reference sections of the recent reviews. Among the 15 selected papers, 11 are original papers (including a total number of 157 patients), one is a systematic review (including 155 patients), one is a meta-analysis (including 359 patients), and 2 describe single cases. All selected papers have been examined by two independent judges, who rated the evidence level of each study in reference to SPREAD criteria [1] (references and class of experience of all selected papers are presented in Appendix 1).

By these means, only one paper (a high quality, statistically homogeneous meta-analysis) has been assigned the maximum level of evidence (1++), whereas four experimental randomized controlled trials achieved 1+ level, one review obtained 2++ score, five original papers 2+ score, one paper 2- score, and three papers have been assigned level of evidence 3. Table I summarizes level of evidence, number of reviewed paper, number of tested patients (experimental and controls), treatment effectiveness, follow-up data, and level of recommendation, separately for each type of rehabilitative method.

Most of the studies published from 2000 to 2007 enrolled patients with mild to severe TBI. Therefore, also the present review, as well as the previous ones, can draw conclusions that cannot be automatically extended to patients with different aetiology.

As it regards the type of rehabilitative method,

five papers employed the Attention Process Training (APT [13]), in isolation or associated to other cognitive or behavioral trainings (Appendix 1). The APT is aimed to stimulate intensive and selective attention by means of tasks presented through different sensorial modalities, following a pre-determined order but with difficulty levels adjustable on the basis of patients' responses. Two studies employing APT have been rated 1+, two studies scored 3, and one scored 2- (Appendix 1). Such evidence would demonstrate that APT, in isolation or combined with other rehabilitative approaches, is effective in the short-term, whereas further studies are warranted to verify its specificity and stability of improvements.

A similar rehabilitative treatment, the computerized AIXTENT program,[14] has been adopted in two studies (Appendix 1), that have been assigned a score 2+ and 3. This program includes several tasks for the different aspects of attention, but differently from APT, the choice and the order of tasks have to be individualized on the basis of single patients' attentional disorder.

Other selected papers did not adopt rehabilitative batteries, but focused on single, specific attentional paradigms such as dual task, task shifting, or working memory tasks (Appendix 1). Two studies on dual task and task shifting achieved an evidence level 2+. The three studies employing working memory tasks achieved evidence levels 2+, 2+ and 1+; in particular, the study by Serino *et al.*[15] reported that a training based on the PASAT paradigm improved working memory and selective attention, with positive outcome generalized to daily life activities (a similar outcome has been reported only in a few other studies). Although such studies, as well as those cited above, can be considered as "direct" restitution trainings, some of them underline that only "strategic" changes may actually reveal successful.[16]

One study, specifically aimed to stimulate different strategies to comply with attentional disorders, is based on the Time Pressure Management method (TPM;[17] evidence level 1+). The TPM is a set of cognitive strategies that can be used to compensate for slow information processing: by means of a series of exercises, patients learn to take sufficient time to solve different tasks adequately. As it addresses strategic aspects, the TPM method seems more suitable than simple restitution trainings to determine generalized improvements in activities requiring high processing rate and memory. Moreover, the study by Fasotti *et al.*[17] is one of the few in which sufficient follow-up data have been provided to ensure stability of improvements over time, although it waits for replication.

In general terms, most of the selected studies report positive outcomes (Table I for a synthesis), although some of them are flawed by some methodological shortcomings (*e.g.*, lack of a control group, possible practice effect, non-superiority of the target treatment *versus* control therapy, possible non-specificity). In particular, in studies employing APT, observed improvements might be ascribed to practice effect or be not specific; moreover, positive outcome might be related to the type of attentional disorder or to its severity. As far as AIXTENT is concerned, it seems to be effective on disorders of intensive attention (*e.g.*, alertness), but it should be assessed on larger and more homogeneous patient samples. The intervention based on dual-task paradigms reports positive outcome with sufficient generalization, but improvements related to spontaneous recovery in the acute stage post-onset cannot be excluded. Also the endogenous task shifting method seems to be effective, but in this case tasks used to evaluate outcome were quite similar to those used during the rehabilitation training and a practice effect cannot be excluded. Last, one study, reporting good outcome after a treatment based on n-back task,[18] is flawed by the small number of treated patients, who also had milder attentional disorders than the control patients.

Comments

In conclusion, the selected papers reported positive outcome, particularly when rehabilitative trainings are tailored on patients' neuropsychological profile and when treatments are based on strategic approaches rather than on repeated execution of specific tasks. The evidence presented here would be consistent with the recent reviews by Cicerone *et al.*[7, 8] and Cappa *et al.*,[9, 10] and would provide at least a partial reply to methodological concerns raised by Lincoln and co-workers,[11] although randomized controlled trials are still strongly needed. Moreover, as stated above, some papers are characterized by some methodological weaknesses, and only a few of them provide long-term follow-up data.

Although several studies reviewed here employed a "direct" approach ("restitution training" or "drill

and practice"), most recent papers would confirm that strategic trainings are particularly effective and allow generalization of improvements (see also [8]); so this approach seems to warrant further studies.

At present, any conclusion has to be limited to patients with TBI, whereas insufficient empirical data are available with respect to treatment of attentional disorders due to different kinds of brain lesions.

Recommendations

EFFECTIVENESS

Patients with acquired brain injury may show attentional disorders that hamper their social life. When attentional disorders are detected by means of standardized test batteries, available evidence demonstrate that specific rehabilitative trainings are effective in reducing such disturbances. With respect to SPREAD criteria, rehabilitative trainings for attentional disorders can receive a Grade A recommendation, based on convergent evidence from four studies with evidence level 1+. However, some methodological limits still exist, among which possible non-specificity of improvements and poor follow-up data.

Effectiveness of trainings has been demonstrated for patients with TBI, particularly those with stabilized disorders or in post-acute stage. Insufficient data are available for patients with different kinds of brain lesion. The interventions stimulating patients' active development of processing strategies seem more promising than treatments based on direct training for specific attentional aspects. Treatments seem to be more successful if planned on the basis of single patients' neuropsychological (and attentional) profile.

FUNCTIONAL OUTCOME

Only about half of the selected papers assessed possible generalization of improvements to daily life activities. In general terms, the best outcome seems to be related to rehabilitative trainings based on a strategic approach.

STABILIZATION OF OUTCOME

Only five studies provided follow-up data, from a minimum of 1 to a maximum of 6 months after the end of treatment (Appendix 1). All such studies demonstrated stability of improvements over time, but in some cases the possible effect of spontaneous recovery could not be evaluated.

Neuropsychological rehabilitation of neglect disorders

Unilateral spatial neglect ("neglect") is a failure to report, respond, or orient to stimuli that are presented contralateral to a brain lesion.[19] Neglect symptoms range from a slowing of responses to contralesional stimuli to a complete lack of awareness of the contralesional half of space, at which point, patients behave as if that half of the world does not exist. Neglect can involve all sensory modalities (vision, audition, somato-sensation) and might affect all sectors of space (personal, peripersonal and extrapersonal space). A left neglect syndrome is very frequently observed in right brain-damaged (RBD) patients in the acute phase: up to 80% of RBD patients present signs of neglect within three months from brain damage.[20] Spontaneous recovery occurs in many patients,[21] but, in one third of the cases, neglect persists and is often severe enough to constitute a major handicap.[22] Thus, neglect rehabilitation is a strong issue for clinical management of patients with acquired brain lesions.

In the last 20 years, several approaches have been proposed to rehabilitate neglect. The different techniques can be distinguished in two major categories of approaches: top-down and bottom-up approaches. Top-down techniques consist of specific exercises aimed at explicitly training the patient to re-orient towards the neglected left side of space. The rationale of these approaches is that neglect is conceived as a failure in automatically orienting attention towards the left side of space; thus, a patient could "learn" to voluntary re-orient leftward in order to compensate for the deficit. On the other hand, bottom-up techniques consist in massively stimulating the patients with information originating from and driving attention towards the left side of space. The rationale of these approaches is that neglect consists in an unbalanced representation of space, with a bias for a hyper-representation of the right space and a hypo-representation of the left space. Thus, critical information from the left space might re-balance spatial representations.

TABLE II.—*Neuropsychological rehabilitation of neglect disorders.*

Level of evidence	Level of recommendation	N papers	N patients (experimental + controls)	Effectiveness	Follow-up
Visuo-spatial orientation					
1++	A	2	33+46	+	No
1+		1	30+23	+	No
2++		4	89+48	+	2 out of 4 studies (+)
2+		3	116+111	+	1 out of 3 studies (+)
3		4	45+16	+(3 out of 4)	3 out of 4 studies (+)
4		1	4	±	No
Prism adaptation					
2++	B	4	43+19	+(3 out of 4)	2 out of 4 studies (+)
2+		2	14+11	+	1 out of 2 studies (+)
3		13	83	±	6 out of 13 studies (±)
4		1	4	±	No
Optokinetic nystagmus					
1+	C	1	11+11	—	No
2+		7	75+53	±	No
3		1	11+11	±	No
Caloric vestibular stimulation					
2+	B	2	22+14	+	No
3		1	1	+	No
Transcutaneous electrical stimulation					
2+	B	4	40+18	+	1 out of 4 studies (±)
Feedback					
2+	C	2	14+14	+	No
3			16+16	+	No
Eye patch					
2+	D	2	19+13	+(1 out of 2)	1 out of 2 studies (–)
–		1	39+15	—	yes (–)
Neuropharmacological treatments					
3	Not recommended	3	9	—	No

In this review, we will present empirical data supporting or not supporting the effectiveness of the different techniques for neglect rehabilitation.

We will review available evidence about: top-down visuo-spatial orientation trainings (VOT); bottom-up trainings, such as prism adaptation (PA), optokinetic stimulation (OKS), caloric vestibular stimulation (CVS), transcutaneous electrical neural stimulation (TENS), bio-feedback and eye patching.

Finally, we will briefly present results of some pharmacological approaches.

Methods

Relevant papers have been collected searching in MEDLINE with the following keywords: [(neglect OR visuo-spatial attention)] AND [(rehabilitation OR treatment OR remediation OR training OR therapy OR intervention OR recovery)] OR [(visual scanning OR prism adaptation OR optokinetic stimulation OR caloric vestibular stimulation OR transcutaneous electrical stimulation OR bio-feedback OR Eye patching)]. In addition, we consulted a number of recent reviews on neuropsychological rehabilitation in general [7-10] and on neglect rehabilitation specifi-

cally.[23-28] Experimental papers, review papers and meta-analyses, published in English up to 2007, were included.

Results

Table II summarizes level of evidence and recommendation, number of reviewed studies, number of tested patients (experimental and controls), treatment effectiveness ("+" indicates a positive outcome; "–" indicates no effect); presence of follow-up assessment (and effectiveness), separately for each rehabilitative technique.

VISUO-SPATIAL ORIENTATION TRAININGS

Visuo-spatial orientation trainings consist in the repetition of a series of exercises (visual scanning, barrage, reading, figures description, figures naming, figures copying) aimed at training the patient to orient towards, and explore the left space.

Fifteen papers describing visuo-spatial orientation trainings have been considered for this review, including a total of 317 neglect patients being treated with this approach (plus 244 control patients). Two papers have been classified with a level of evidence 1++, one paper with 1 +, four papers with 2++, three papers with 2+, four papers with 3 and one paper with 4 (Appendix 1).

A general principle of visuo-spatial orientation approach is that exercises' difficulty increases along the training. Length, frequency and number of sessions vary between the different studies. Notably, effective trainings have been administered for at least 4-8 weeks of daily sessions. Some methods also include external cues placed in the left space to attract and anchor patient's attention.[29] In general, most effective studies have used a number of different exercises, varying materials and tasks, in order to maximize the probability of generalizing the training effects during everyday life activities. However, evidence is controversial about the real generalization of the trainings' effects to untrained visuo-spatial abilities and to patient's functional recovery. Follow-up data are available up to six months from the end of treatment.[30] Some papers explored the effectiveness of visuo-spatial orientation trainings associated with other techniques (*e.g.*, with OKS [31], with TENS [32]), but no studies reported additional benefits due to the combination of two rehabilitation methods.

PRISM ADAPTATION (PA)

The PA procedure consists of the repetition of a series of pointing movements while the patient wears prismatic lenses that shift the visual field towards the right. To compensate for this optical displacement, the patient has to orient his/her pointing movement toward the left of visual space, resulting in a leftward drift of sensorimotor coordinates. Such visuomotor adaptation process can modify high-level spatial representations, thus improving neglect.[27]

Twenty papers about effectiveness of PA for neglect rehabilitation have been considered, involving a total of 143 patients (plus 30 patient controls). Four papers have been classified 2++, two papers 2+, thirteen papers 3 and one paper 4 (Appendix 1). Duration of PA administration varies between the different studies: most papers (14) have analyzed the effect of 1 session of PA; in 1 paper PA has been repeated for three consecutive days, in three papers, for two weeks of daily sessions. Most of the studies demonstrate that a single session of PA is effective to recover several neglect symptoms (visual exploration and reading;[33] eye movements;[34-36] mental imagery;[37] touch [38]), in acute and chronic patients (but see also Rousseaux *et al*.[39]), but the training effects vanish in 24 hours.[40] However, the repetition of PA sessions (*e.g.*, two weeks of daily PA treatment) has been shown to induce a stable recovery of neglect, tested up to six months from the end of the treatment.[41] No data at the moment support the generalization of the benefit due to PA to the patient's motor and functional recovery.

OPTOKINETIC STIMULATION (OKS)

OKS involves the presentation of a visual moving stimulus (*e.g.*, random dots moving leftward on a background) [42] which triggers a nystagmus in which the slow phase is coherent with the movement of the triggering stimulus (leftward) and the quick phase reverts eyes to the initial point of fixation.[43] The rationale of using OKS for neglect rehabilitation is inducing a leftward deviation of eye positions in order to compensate for the patients' rightward bias.[44] Nine studies testing the effects of OKS on neglect rehabilitation have been considered, testing a total of 97 neglect patients submitted to OKS and 119 patients or healthy controls. One study has been classified 1+, seven studies 2+ and one study 3 (Appendix 1).

Different studies have manipulated the shape,[42] size, number,[45] type,[44] and movement velocity of visual stimuli.[46] The effects of OKS on different measures of spatial attention (line bisection, visual scanning, reading, visual perception) have been evaluated. Eight studies have tested the effects of one day of OKS, while two studies have repeated the procedure for up to six weeks. No study has tested the long-term effect of OKS by means of follow-up assessments. The 1+ class study [31] failed to show an additional effect of OKS to the neglect rehabilitation induced by visuo-spatial orientation training. Studies classified 2+ have shown some amelioration in standard measures of neglect, but the persistence in time, the functional outcome and therefore the clinical value of the benefits induced by OKS ought to be demonstrated.

Caloric vestibular stimulation (CVS)

The application of cold water to the left ear canal produces a vestibulo-ocular reflex in which the slow phase of the nystagmus moves toward the stimulated, left ear. Head turning is also induced in the same direction. A similar, although weaker, effect, in the reverse direction, can be obtained by applying warm water to the opposite ear.[47] Therefore CVS has been used in neglect patients to shift eye and head position towards the left side of space, in order to reduce the rightward attentional bias of neglect.[48]

We considered three papers testing the effects of CVS on a total of 25 neglect patients (plus 14 patient and healthy controls). Two studies have been classified 2+ and one study 3 (Appendix 1). A transient amelioration of visual exploration following CVS has been demonstrated, but the effect vanishes soon after the end of the stimulation; thus the clinical relevance for neglect rehabilitation through CVS is questionable at the moment.

Transcutaneous electric stimulation (TENS)

TENS consists in applying a low-voltage electrical stimulation to the contralesional side of the patient's body (normally at the neck muscles, so that this procedure is also called neck vibration) in order to induce a passive activation of the neglected side of the body, thus potentially compensating for the rightward bias of neglect.[49, 50] Four papers testing the effectiveness of TENS on a total of 40 neglect patients (plus 9 patient and healthy controls) have been considered and classified as 2+ (Appendix 1). The four studies differ for time from brain damage of included patients, time and intensity of stimulation and number of sessions. They report some amelioration of visual exploration, drawing, mental imagery and hemianesthesia after TENS applied to the left neck muscles. However, not enough evidence is available on the duration of these benefits and their generalization to the patient's clinical outcome.

Feedback

The rationale of this approach is that normally neglect patients are not aware of their spatial deficits. However, if during exploration, they are presented with appropriate sensory (visual,[51] or proprioceptive [52]) stimulation about their pathological behavior, they can use such feedback information to correct their current and potentially future performances. Three studies (Appendix 1) have tested the effectiveness of feedback procedures on a total of 30 neglect patients (plus 14 patient controls). Two papers have been classified as class 2+ studies and one study as class 3. Results are generally coherent in showing a positive effect of such procedures for the task in which feedback is actually provided, but no data show generalization to untrained visuo-spatial abilities, or to the patient's functional outcome.

Eye patch

Eye patch technique consists in depriving the patient of visual information for the right hemispace by occluding the nasal hemiretina of the right eye and the temporal hemiretina of the left eye, or by occluding the right eye. In this way, the neglect attentional bias towards the right space should be reduced, by decreasing right-sided sensory inputs,[53] and the representation of the left space should be enhanced,[54] by reducing the competition for attentional resources between left and right stimuli. Three studies investigating the effects of eye patch in neglect rehabilitation have been considered, testing 58 patients (plus 28 patient controls). One study did not report any evidence of neglect improvement after eye patch, whereas the other two studies (both classified as class 2 evidence) report an amelioration in some visuo-spatial abilities, but did not test

whether these effects are stable in time or generalize to the patient's functional outcome (Appendix 1).

Neuropharmacologic treatments

Pharmacologic approaches to neglect consist in administering dopamine-enhancing medications. The rationale of the approach is that in animal models, the severity of neglect correlates with the degree of dopamine depletion,[55] therefore a similar neurotransmitter deficit might be present in human patients and could be compensated by appropriate drugs administration.[56] Three studies on the effectiveness of pharmacological treatment of neglect have been considered. Two of them are reports of single cases, and one study tested seven patients, with no control group; thus, all of them have been classified as class three studies (Appendix 1). Bromocriptina or metylphenidate were administered, but no improvement (in fact, some worsening) of patients' visuo-spatial abilities was reported.

Comments

Several methods have been proposed to treat neglect syndrome. Most of the considered studies describe experimental investigations testing the possibility of using any given technique to induce some neglect recovery, whereas fewer clinical trials (appropriately testing the effectiveness of rehabilitative programs for neglect patients) are available. Thus, many of the available results are interesting from a theoretical point of view but their direct value for the clinical practice is questionable. Having said that, at the best of the available evidence, some important conclusions can be drawn concerning the effectiveness of the different techniques for neglect rehabilitation.

Visuo-spatial orientation trainings have received satisfactory support as effective methods for neglect treatment, even if it is not totally clear how much the treatment effects directly generalize to patient's abilities in everyday life. The present evidence confers level A recommendation to visuo-spatial orientation trainings for neglect rehabilitation.

More recently, the most promising approach to neglect is represented by the PA technique. This method is easy to apply, well tolerated by patients, and has been shown to induce a long lasting recovery of visuo-spatial abilities. At the time of the present query of the literature, these effects were not supported by any RCT trials, and therefore the available evidence confers a level B recommendation to PA. However, studies published after 2007 have also provided RCT-based evidence [57, 58] (but see also Turton *et al.*[59])

Some reports support the view that CVS and TENS improve neglect symptoms, but these benefits are limited to the time of application of the stimulation, thus it is not clear whether and how these treatments could be really used in the clinical practice. The recommendation level for both CVS and TENS is C.

Feedback methods have shown positive effects on the task used during treatment, but no generalization to untrained activities. The level of recommendation is C.

Results about the effectiveness of OKS and Eye patch techniques are not so consistent, resulting in a level D recommendation.

Finally, pharmacological treatments have been shown to be ineffective, or even negative, for neglect patients; thus, at the moment, they are not recommended.

Neuropsychological rehabilitation of acquired dysexecutive disorders

Lesions in prefrontal areas may cause deficits in cognitive and behavioral regulation,[60] severely affecting patients' outcome, impeding reintegration in their familiar social and work environment, even when their instrumental cognitive skills are not affected by any disorder (such as aphasia, agnosia, apraxia or deficits of visuo-spatial representation).

Deficits following prefrontal lesions are usually referred to as dysexecutive disorders.[61, 62] They involve difficulties in many areas, including planning daily life activities, prospective memory, selection of appropriate behaviors and monitoring actions and behaviors. Dysexecutive disorders are strongly correlated with (and often difficult to distinguish from) attention deficits and behavioral disorders.

Methods

The present review of studies on the rehabilitation of acquired dysexecutive disorders is based on papers indexed in the following databases: MEDLINE, PsychINFO, EMBASE, CINAHL. We used the following key words to search for papers: "acquired brain

TABLE III.—*Neuropsychological rehabilitation of acquired dysexecutive disorders.*

Treatment – Setting	Level of evidence	Level of ecommendation	N papers	N patients (experimental+ controls)	Effectiveness	Follow-up
Page maker	1++	A	1	143	+	+
Goal management therapy (single session)	1+	B	1	16+12	+	No
Goal planning – Individual or group training	1+	B	1	54+56	+	No
Problem solving therapy (with or without PC)	2++		1	15	+	No
Social communication – Individual training	2+		1	26+26	+	+
Time organization – Individual training	2+		1	20	+	No
Social skill training	2+		1	25+12	+	No
Autobiography recall (single session)	2+		1	15+15	+	No
Periodic alerting signal	2+		1	10+24	+	No
Problem solving therapy	2+		1	27+19	+	No
Goal planning approach	3		1	1+1	+	+
Specific training (kitchen)	3		1	54	+	No
Categorization (abstract thinking)	3		1	10+13	+	No
Specific training (internet)	3		1	7	+	No
Interactive strategy modelling	3		1	20	+	+
Planning training – At home	3		1	3	+	(+)
Specific training (writing notes)	3		1	1	+	No

injury", "traumatic brain injury", and "brain injury"; each was combined using the [AND] logic operator with the following key words: "executive/dysexecutive" [OR] "problem solving", [OR] "goal management"; [AND] "deficit", [OR] "disorders"; [AND] "treatment", [OR] "intervention", [OR] "rehabilitation", [OR] "therapy". In view of the presence of various systematic reviews in this area,[7-10] search was restricted to studies published in English from 2000 to 2007. Other papers were identified using the references reported in the papers that emerged from the abovementioned databases.

A selection of the identified papers was made using the following exclusion criteria:

a. interventions limited to occupational (or vocational therapy or training of specific skills) and job coaching aimed at job reintegration;

b. interventions aimed at training caregivers and relatives to manage patients with dysexecutive disorders;

c. descriptions of theoretical models and methods that do not report quantitative data;

d. non-systematic reviews, clinical-epidemiological studies, proceedings, lectures and monographic publications.

Results

We identified 56 papers of potential interest. We excluded 11 papers because they were considered in the section on rehabilitation of attention disorders. We excluded 23 papers because they did not completely fit with the aim of present review and two papers because they described single-case treatments and did not report adequate measures of treatment effects or details about the applied treatments. One study on the effectiveness of a computerized aid was excluded because it did not provide sufficient information about the type of treatment administered. Finally, two papers were excluded be-

cause they presented no systematic review of the literature. The remaining 19 papers consisted of two literature reviews and 17 original studies.

Table III summarizes level of evidence and recommendation, number of reviewed studies, number of tested patients (experimental and controls), treatment effectiveness, and follow-up data, separately for each type of rehabilitative method.

The 17 original studies included a total of 447 subjects who had undergone treatment for the reduction of dysexecutive disorders (Appendix 1). In all but one study [63] the treatment was administered to people with TBI. Although treatment effectively reduced dysexecutive disorders in all studies, very few verified the stability of the improvements obtained by follow-up testing.

Rehabilitation goals, (as well as methodologies, type of treatment and measures of treatment effectiveness) varied greatly among studies. Furthermore, most studies used training that lasted for several sessions. Other studies, however, used treatments limited to a single training session.

Due to the great variability among studies, it is difficult to estimate the amount of evidence available on treatment effectiveness. Seven of the 17 original studies were classified as level 3. Some of them described treatments aimed at improving a specific ability. In these cases, the training referred to rehabilitation of executive functions, because it was aimed at obtaining better planning of daily life activities (*i.e.*, learning to subdivide each activity into goals and sub-goals). Seven studies obtained class 2+ or 2++ scores. Three studies (adopting controlled, randomized clinical trials) obtained class 1+ or 1++ scores. The first study [64] describes goal management training (GMT), a one-session treatment aimed at improving the planning of daily life activities; efficacy of GMT was assessed by means of a paper-and-pencil test reproducing an ecological situation. The second randomized and controlled study [65] investigated the efficacy of a different type of training aimed at improving the planning of daily life activities. The training was administered to groups or to single patients at home and its effects were assessed by means of an ad-hoc developed test. The third study [63] shows the efficacy of training in the use of an electronic planner to improve both prospective memory and planning of daily life activities. The improvements were stable at a 2-month follow-up.

Conclusions

Results of the present review confirm those of two recent, systematic reviews.[8, 66] Therefore, we can conclude that, at present, several randomized controlled studies demonstrate the efficacy of some treatments in reducing dysexecutive disorders. Except for the study by Wilson *et al.*,[63] all others report treatment effectiveness in patients who suffered traumatic brain injuries, and any conclusions about the efficacy of rehabilitation of dysexecutive disorders have to be limited to this population.

The evidence level of treatments aimed at rehabilitating the planning of daily life activities allows recommending their use in rehabilitating dysexecutive disorders. Up until now, the efficacy of treatments aimed at rehabilitating specific activities has not been rigorously demonstrated. Use of a computer in the rehabilitation of dysexecutive disorders does not result in increased treatment effectiveness.[67]

Some limitations must be reported. First, in most of the reviewed studies a small number of patients (and often single cases) were investigated. Although our conclusions are based on single studies of very good methodological quality, which have undergone rigorous controls, at the moment converging evidence on the efficacy of a specific treatment is still lacking. Effectiveness of the above-described treatments for use in cases of dysexecutive disorders with an aetiology, other than brain injury, still has to be demonstrated.

Only a few of the most recent studies have attempted to verify generalization of improvements to daily life. Furthermore, stability of improvement after the end of treatment has not been thoroughly investigated. Indeed, these two aspects certainly deserve greater attention in future studies.

Recommendations

Effectiveness

Due to the lack of convergent data, the present recommendations are based on individual, well-controlled studies.

On the basis of the randomized and controlled study (level of evidence 1++) by Wilson *et al.*,[63] training in the use of an electronic planner to improve the daily life activities in brain-injured or cerebro-vascular patients receives a grade A recommendation. This study also demonstrated that the

improvements were stable and still present seven weeks after the end of the training, and that they extended to daily life activities.

The treatments described in the two studies that received a 1+ level of evidence received a grade B recommendation. In particular, Powell *et al*.[65] demonstrated the efficacy of training aimed at improving planning in patients with non-severe TBI, testing the effect in daily life activity. The GMT, presented in the second level 1+ study,[64] seemed to effectively improve planning abilities in traumatic brain-injured patients, but its generalization was no demonstrated because efficacy was tested only by means of paper-and-pencil tests. However, taken together the results of the two level 1+ studies indicate the effectiveness of the treatment of planning deficits in brain-injured people. Although evidence from the remaining studies suggests their potential impact in reducing dysexecutive disorders, it does not allow considering any of the specific treatments effective according to the SPREAD standards.

Functional impact

Two of the studies with a high level of evidence [63, 65] verified the generalization of improvements to daily life, suggesting that the treatment of dysexecutive disorders has a relevant functional impact. However, this point deserves further study.

Stability and long-term efficacy

Although none of the studies reported a full evaluation of stability and long-lasting effectiveness, some of the well-controlled ones evaluated the stability of effects some weeks after the end of treatment. Therefore, further studies are needed to verify the stability of acquired improvements after treatment.

Neuropsychological rehabilitation of patients with mild TBI

In both intensive care [68] and rehabilitation,[69] TBI is classified as severe, moderate or mild depending on the level of unconsciousness in the acute phase on admission to hospital. This level is commonly measured with the Glasgow Coma Scale: mild TBI falls within the range of 13-15 on this scale. Other clinical parameters used to define the level of mild TBI are length of loss of consciousness, or coma, and length of post traumatic amnesia (PTA). To be classified as mild TBI, length of unconsciousness must be <30' and length of PTA must be contained within <24 hours.[70]

The long-term recovery of neuropsychological disorders following mild TBI is still a controversial topic in the literature, even though scientific articles have been published for decades. Although most cases of mild TBI completely recover, in some patients the neuropsychological, behavioral, psychological and psychosocial outcomes persist over time.[71]

Post-trauma symptoms vary and may involve impairment of physical, emotional and cognitive functions.[72] The most common physical symptoms include headache, nausea, dizziness, photo-sensitivity, noise intolerance, sleep disorders and persistent pain in the neck and shoulders. Emotional disorders include irritability, anxiety, changes in mood and personality, fatigue and depression. Cognitive symptoms include, above all, difficulties in concentration, memory (both visual and verbal as well as at work), intellectual and cognitive processing, verbal fluency, executive functions and inability to carry out tasks with the same level of skill as before TBI.[73] In cases of mild TBI, it is important to establish whether cognitive deficits are a direct consequence of brain trauma (*e.g.*, in the presence of diffuse axonal damage) or can be considered secondary to mood disorders such as irritability, anxiety and depression. It is also important to determine whether they are accentuated by factors such as pain, stress, and/or matters related to possible compensation claims.[74]

Evaluation of mild TBI should focus on the various aspects that may be compromised and should be carried out using neuropsychological tests (for attention, memory and executive functions), scales to assess behavior and a checklist of somatic, cognitive and emotional symptoms for both patient and caregiver.[71] Furthermore, evaluation in a rehabilitation setting should include testing to determine the impairment level of abilities and social skills.

Because of the rapid recovery of most patients and the possibility that patients will develop hypochondriacal symptoms (*i.e.*, other than the financial compensation preoccupation, the so-called adoption of the sick role), a thorough evaluation is advisable if symptoms persist beyond the first month following the traumatic event.[75] Unless patients completely recover from symptoms before a year has passed

from mild TBI, the evaluation should be repeated monthly for up to a year after the traumatic event.[73]

Not all mild TBI patients require rehabilitation. In fact, there are reports in the literature that, three months from the traumatic event, neuropsychological deficits and physical and emotional symptoms may persist in 2% to 25% of cases. Even if long-term outcomes persist in a limited number of mild TBI cases, the mild TBI group has an overall high incidence. Cassidy *et al.*[76] reported data pertaining to the USA: 100-300 new cases out of 100 000 inhabitants are admitted to hospital every year. This value increases to 600/100 000 when non-hospitalised patients are considered.

Therefore, evaluation and rehabilitation of patients suffering mild TBI outcomes should constitute an important part of any health protocol. The complex pattern of post-trauma symptoms in patients with TBI and the incidence and social relevance of the phenomenon underscore the interest for assessment and rehabilitation programs by health planning and policy.

Three months after mild TBI, neuropsychological deficits and physical/emotional symptoms persist in a small number of patients (less than 1/3), who should be monitored and assessed over time (cognitive tests, behavioral scales, symptom checklists) and who would benefit from the following types of treatment:

1. neuropsychological rehabilitation;
2. holistic rehabilitation;
3. education programs.

Neuropsychological rehabilitation programs aim at improving functions, identified using cognitive reference tests whose purpose is to recover as much as possible of that function and verify the possibility of transferring the result to other untreated functions. Here, we focus on trainings aimed at multiple cognitive functions (the reader is referred to the other sections of this review for trainings specifically tuned on either attentional or dysexecutive deficits).

Holistic rehabilitation, on the other hand, takes a different approach. Contrary to the hackneyed use of the term "holistic", certain criteria have to be respected if an intervention is to be considered holistic. The presence of a multidisciplinary team or the use of a wide range of interventions (psychotherapy, cognitive training, occupational therapy etc.) is not enough to for an intervention to be considered holistic. The theory of rehabilitation on which holistic interventions are based (translated from the clinical practice of Ben-Yishay *et al.*,[77] Christensen *et al.*,[78] and Prigatano [79]) focuses on the interactions between various "cognitive models", and between these models and the patient's living environment and emotional reactions. The patient's individual problems are not seen singly but rather all together. This also requires that particular attention be placed on the entirety of the psychic phenomena from diagnosis to intervention. No single cognitive model or emotional aspect is treated. Instead, individuals with all their cognitive changes and emotional reactions are treated in their natural context. These programs often take place outside hospital facilities, in a natural setting where, from the very beginning, the treatment is directed toward encouraging social participation, including reintegration into the workplace and improving the quality of life of patients and their families. A description of these programs can be found in Ben-Yishay,[80] Kaipio *et al.*,[81] and Zide and Ben-Yishay.[82]

Results of holistic programs have shown uniform improvement in the chronic phase and in treatment outcomes regarding resumption of activity in patients with all levels of TBI, and this improvement remains stable even for years after completion of the programs.[83] Besides increased resumption of activity, results also show improvement in other aspects of daily living, such as greater independence [84] and increased emotional stability.[85]

Education programs for patients and their caregivers constitute another approach for rehabilitating the cognitive disorders of patients with symptoms following mild TBI. These can be carried out orally (with written information or using a video) in single or repeated sessions with one or more members of the rehabilitation team; furthermore, these programs can be ready-made or can be individually tailored to suit the needs of the patient.

Methods

Identification of rehabilitation programs for mild TBI was carried out by means of bibliographical research using various research motors: PubMed, Medline, PsychInfo, Scirus and Cochrane, selecting all works published before 2007.

The key words common to the three sub-topics were: "mild TBI", "mild CHI" (TBI: Traumatic Brain Injury; CHI: Closed Head Injury).

TABLE IV.—*Neuropsychological rehabilitation of patients with mild traumatic brain injury (TBI).*

Level of evidence	Level of recommendation	N papers	N patients (experimental + controls)	Effectiveness	ADL	Follow-up
Neuropsychological rehabilitation of patients with mild TBI						
1+	B	2	276+131	+ (1 out of 2)	Yes (1 out of 2)	Yes
2-		5	79+50	+	Yes (1 out of 5)	Yes (1 out of 5)
3		2	2	+	No	Yes (1 out of 2)
Neuropsychological rehabilitation of mixed groups including mild TBI						
1+	B	2	99+110	+	Yes	Yes
2+		1	21+21	+	Yes	No
2-		1	34	+	Yes	Yes
Holistic rehabilitation in patients with mild TBI						
1+	B	1	97 (mild)+94	+	Yes	No
2+		4	219 (mixed)+17	+	Yes	Yes (3 out of 4)
Education programmes for patients with mild TBI and caregivers						
1+	A	4	220 (mild)+263	+	Yes (3 out of 4)	Yes
1+		1	184 (mixed)+130	+	No	Yes

These key words were combined with the following key words:

— for neuropsychological rehabilitation: "neuropsychological rehabilitation", "cognitive rehabilitation", "rehabilitation", "treatment";

— for holistic rehabilitation: "holistic rehabilitation", "milieu rehabilitation";

— for education of the patient or caregiver: "education", "intervention".

From the studies found, we excluded those referring to TBI in general terms, in developing age, in sports and those on moderate, severe or very severe TBI. We also excluded books, chapters or reviews that did not provide detailed reports on the literature examined.

Results

NEUROPSYCHOLOGICAL REHABILITATION

Table IV summarizes level of evidence and recommendation, number of reviewed studies, number of tested patients (experimental and controls), treatment effectiveness, activities of daily living (ADL) and follow-up data separately for each type of rehabilitative method. Notably, because it was not easy to find material focussing only on patients with mild TBI, the search often included mixed groups (TBI mild and others). Therefore, in Table IV studies on mild TBI (N.=11) and studies on different types of TBI including mild TBI (N.=7) are presented separately.

Studies on mild TBI.—Our search revealed nine experimental studies that focused only on patients with mild TBI (Appendix 1). These studies were published between 1995 and 2007. Eight studies were prospective and three retrospective.[86-88] Note that most studies did not report blindness to the aims of the study and/or treatment carried out by the evaluator, therapist or patient: one study reported blindness of the evaluator,[89] and none blindness of the therapist.

The size of the patient population examined varied from study to study and ranged from 1 to 395 patients. There were two single-case studies.[90, 91] Only two studies used a randomized research design.[89, 92] The time lapse between onset and beginning of treatment was most often about one year, even though the range was large (from three weeks to six years). Length of treatment also varied greatly: from 12 hours [93] up to 155 sessions (mean 1.88 sessions/week).[88] Sessions generally lasted about an hour.

The aims and types of treatment were different in each study. Studies examined the efficacy of a wide range of rehabilitation programs (from integrated programs providing interventions of "direct" cognitive training, to programs teaching techniques and compensatory strategies, psychotherapeutic and/or

cognitive-behavior interventions, and occupational therapy [87]). Furthermore, the studies showed great variability in the choice of evaluation tools, making it difficult to integrate the results obtained by the individual studies. All studies provided individually-tailored treatment.

Studies including various types of TBI.—We found four experimental studies: two had a mixed group of mild and moderate TBI,[94, 95] one a group composed of mild and severe TBI,[96] and only one study a mixed group of mild, moderate and severe patients.[97] Here, the focus obviously shifted from indices of level of severity linked to the traumatic event to indices of severity of the outcome.

The studies selected were published between 1972 and 2007: two were prospective in design and two retrospective.[94, 96] None of the studies reported the blindness of the evaluator or the therapist. The size of the patient population examined ranged from 178 to 314 cases. Two out of the four studies used a randomized research design.[95, 97]

Also in this group of studies, the rehabilitation programs varied greatly; studies examined the efficacy of wide-ranging rehabilitation programs through integrated programs providing occupational, speech and neuropsychological therapy, like Goranson *et al*.[94] Three studies used individually-tailored treatment. Sander and co-workers [96] used both an individual and a group approach. All studies showed great variability in the choice of evaluation tools.

Holistic rehabilitation.—Almost all studies on holistic programs were carried out on chronic patients and mixed groups of patients. The length of the program varied from six weeks [84] to seven months,[98] with high attendance and prolonged length of sessions (a minimum of four days per week for at least four hours a day). Evaluation of the outcome of these programs focused on aspects of social participation: all works listed aimed at return to work and/or retaining work. Treatment mainly included group activities, but also some individual psychotherapy.[99]

Regarding return to work, the outcome was usually measured based on a list on which work was classified as full-time, part-time, sheltered, voluntary, and unemployed. All studies showed an increase in work activity from pre- to postintervention. The three class 2+ studies [84, 98, 100] had a follow-up period that varied up to three years. In the study with a case controlled design, which compared the experimental group with a group of patients involved in an individual rehabilitation program, the holistic intervention produced greater return to work in the patient than in the control group.[100] These authors, however, did not specify the activity of the control group and did not carry out a statistical analysis on the variables affecting the lack of return to work.

Rattok *et al*. (class 2+ study) [85] analysed the impact of the various components of a rehabilitation program on different aspects of social outcome, not only work outcome. The authors divided the 56 patients into three groups of different composition of the single elements of the intervention, and concluded that a well-balanced combination of cognitive, psychosocial and interpersonal interventions did not increase the likelihood of return to work at 3 and 9 months as compared to a single treatment; on the other hand, the combined treatment was more effective in improving psychological and interpersonal aspects (self esteem, empathy).

Education programs for patients and caregivers

A systematic PubMed search allowed us to identify five studies on patients with mild TBI (all classified as 1+ in accordance with SPREAD) that demonstrated the benefits of an education program (Appendix 1).

Ponsford and co-workers [101] assigned 202 patients with mild TBI to two different groups: in the "intervention group" (N=79) the patients were contacted within 48 hours. They were given an informative manual on the symptoms that may occur following mild TBI, their possible development over time, and suggestions of various coping strategies to adopt. The patients included in the "non-intervention group" (N=123) only received standard treatment and were not given the informative manual. The individuals who were not immediately contacted after the traumatic event (and did not receive the informative manual) complained of more symptoms (sleep disorders and anxiety) three months after the trauma compared with the patients who had received the other type of intervention.

Wade *et al*.[102] carried out a randomized study in which 7-10 days following trauma the experimental group (N=184) received supplementary assistance in which the occupational therapist and clinical psychologist, both experts in treating patients with mild TBI, interviewed patients who asked for meetings.

After the evaluation phase, the experimental group, and family members, if it was deemed necessary, received information, advice and support for the management of postconcussion syndrome aimed at reducing the effects of stress linked to cognitive disorders and at helping the patient gradually return to normal activities. Six months after brain injury, the patients belonging to the experimental group showed less disability in social outcomes, and complained of fewer postconcussion symptoms compared with the group that had not received the supplementary intervention.

Paniak *et al.*[103] administered two types of treatment to patients with mild TBI: one group (N=60) received a single session of intervention in which the trauma was "legitimized" and received information regarding the common symptoms and clinical signs linked to mild TBI as well as suggestions on how to cope with the problems. They were encouraged to resume their normal activities as quickly as possible and were reassured about their prognosis. The other group (N=59) received the same treatment but an extra three or four hours of neuropsychological and personality evaluation, consultation with a physiotherapist, specialised in the treatment of postconcussion symptoms, a session in which the patients were given the results of their tests and a further treatment of deficits they had complained of following mild TBI. Treatment also included physical and psychological interventions and, if deemed necessary, access to a multidisciplinary treatment program. The authors found that three-four months from baseline, the two groups improved in the same way and showed no differences regarding functional and occupational variables or relative symptoms. Paniak *et al.*[104] confirmed the results a year later: there were no differences in outcome 12 months after TBI. Therefore, it seems that providing the patient with a brief "education" program in a single session, as quickly as possible following TBI, may be as useful as intensive and prolonged treatment.

Mittenberg *et al.*[105] reported similar results: the "intervention group" was given an informative manual regarding postconcussion symptoms and sessions with a therapist to analyse the nature and incidence of the symptoms, based on a cognitive/behavioral interpretation model. Furthermore, they provided techniques to reduce symptoms and instructions on gradual resumption of previous activities; the "control group", instead, received standard hospital treatment and written instructions at discharge. The experimental group showed a reduction of frequency, length, and severity of symptoms.

Comments

Neuropsychological rehabilitation

The literature on neuropsychological rehabilitation in patients with mild TBI is scanty. In fact, we found and classified a total of 13 studies. However, there are studies (limited in number and quality) that attempted to develop specific programs for patients with mild TBI (N.=9). In these studies, the rehabilitation programs were often presented with models that are not easy to reproduce. Moreover, each work examined a different approach or rehabilitation program, making it difficult to compare them.

Furthermore, the variability in the choice of evaluation tools makes it even more difficult to integrate the results obtained in the various studies.

The review of the literature also demonstrated the scarce attention given to methodological aspects such as randomization of study design (four studies out of 13), the need for a follow-up to verify the maintenance of therapeutic effects, and blindness as to the goals of the study and/or treatment carried out by the evaluator, therapist and/or the patient (few studies report this information).

Finally, the distinction between mild, moderate and severe, which is most often linked to clinical conditions in the acute phase, is not satisfactory from the point of view of rehabilitation, where the focus is on the severity of the neuropsychological outcome in the post-acute or chronic phases. Nevertheless, it has been shown that the severity of post-acute and chronic disorders does not necessarily correlate with the severity of TBI in the acute phase. Furthermore, the need for rehabilitation for post-concussion disorders may be the same regardless of the severity of TBI in the intensive phase.

Holistic rehabilitation

Regarding holistic rehabilitation, the lack of any prospective randomized clinical trials (RCT) must be pointed out. The rather low number of patients in the various groups (experimental and control), coupled with the lack of replication at other research centres, can be considered additional shortcomings.

EDUCATION/INFORMATIVE PROGRAMS

The works reviewed demonstrated the usefulness and effectiveness of educational programs for patients with mild TBI and their family members in reducing or preventing symptoms, but not necessarily improvement of neuropsychological functions. In any case, the programs should start as early as possible [103] and be simple, precise and adaptable to the individual and, if possible, should be presented, in written form.[102]

Recommendations

EFFECTIVENESS OF THE METHOD

Neuropsychological rehabilitation.—Class of evidence in accordance with SPREAD tables on mild and mixed with mild TBI ranges from 1+ to 3: for mild TBI there are two class 1+ studies, five class 2-, and two class 3 studies; thus, the recommendation level is B. For mixed with mild TBI there are two class 1+ studies, one class 2+ and one class 2- studies; thus, the recommendation level is B.

Mainly as a result of the scarcity of research carried out on treatment type, the recommendation level for specific neuropsychological treatment for patients with mild TBI is still rather limited. The quantity and quality of research is still too scarce to allow us to draw sound conclusions. Similar conclusions were drawn also in the reviews of Comper *et al*.[106] and Ponsford.[74]

Holistic rehabilitation.—The body of evidence justifies a recommendation level of B: the studies are consistent with one another on a class 2+ level, to which another class 1+ may be associated.[99] This evaluation is limited to the cases typical of these programs: TBI in the chronic phase, ages ranging from 18 to 55 years, patients who are relatively independent as regards ADLs, no psychiatric illness or substance abuse, and functional communication.

Education programs for the patient and the caregiver.—All five works on mild TBI are classified as 1+; so, their recommendation level is A.

Functional relapse of therapy

NEUROPSYCHOLOGICAL REHABILITATION

Assessment of ADLs in studies on neuropsychological rehabilitation is present in six out of a total of 13 studies: three class 1+ studies,[89, 95, 97] one class 2+ study,[94] and two class 2- studies.[88, 96]

HOLISTIC REHABILITATION

All studies on holistic rehabilitation reported assessment of ADLs and showed substantial improvements at follow-up in numerous participation variables such as functional independence in ADLs [84, 98, 100] and involvement in free-time activities.[84]

EDUCATION PROGRAMS FOR PATIENTS AND CAREGIVERS

ADLs were assessed in only 3 out of 5 studies.[103-105]
Stability of therapeutic effects over time

NEUROPSYCHOLOGICAL REHABILITATION

The six-month follow-up of studies on neuropsychological rehabilitation was reported in seven studies (class of evidence 1+;[89, 92, 95, 97] class of evidence 2-;[87, 96] class of evidence 3 [91]).

HOLISTIC REHABILITATION

Three out of five studies on holistic rehabilitation [84, 98, 100] reported a follow-up of at least eight months [84] up to a maximum of 36 months.[100]

EDUCATION PROGRAMS FOR PATIENTS AND CAREGIVERS

The six-month follow-up was reported in all 5 studies, from a minimum of 3 months following termination of treatment to a maximum of 12 months.[103]

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APPENDIX I

Reference	Level of evidence
Neuropsychological rehabilitation of attentional disorders	
Interventions based on attentional batteries	
APT (Individual)	
Sohlberg MM, Mclaughlin KA, Pavese A, Heidrich A, Posner MI. Evaluation of attention process training and brain injury education in persons with acquired brain injury. J Clin Exp Neuropsychol 2000;22:656-76.	1+
Palmese CA, Raskin S. The rehabilitation of attention in individuals with mild traumatic brain injury, using the APT-II programme. Brain Inj 2000;14:535-48.	3
Pero S, Incoccia C, Caracciolo B, Zoccolotti P, Formisano R. Rehabilitation of attention in two patients with traumatic brain injury by means of 'attention process training'. Brain Inj 2006;20:1207-19.	3
APT (Individual) with cognitive-behavioral psychotherapy	
Tiersky LA, Anselmi V, Johnston MV, Kurtyka J, Roosen E, Schwartz T, et al. A trial of neuropsychologic rehabilitation in mild-spectrum traumatic brain injury. Arch Phys Med Rehabil 2005;86:1565-74.	1+
APT (Individual) with compensatory strategies	
Boman I-L, Lindstedt M, Hemmingsson H, Bartfai A. Cognitive training in home environment. Brain Inj 2004;18:985-95.	2–
AIXTENT (Individual)	
Sturm W, Fimm B, Cantagallo A, Cremel N, North P, Passadori A, et al. Specific Computerized Attention Training in Stroke and Traumatic Brain-Injured Patients: A European Multicenter Efficacy Study. Zeitschrift für Neuropsychologie 2003;14:283-92.	2+
Sturm W, Longoni F, Weis S, Specht K, Herzog H, Vohn R, et al. Functional reorganisation in patients with right hemisphere stroke after training of alertness: a longitudinal PET and fMRI study in eight cases. Neuropsychologia 2004;42:434-50.	3

Reference	Level of evidence
Interventions based on specific tasks	
Dual task (Individual)	
Stablum F, Umiltà C, Mogentale C, Carlan M, Guerrini C. Rehabilitation of executive deficits in closed head injury and anterior communicating artery aneurysm patients. Psychol Res 2000;63:265-78.	2+
Endogenous task-shifting (Individual)	
Stablum F, Umiltà C, Mazzoldi M, Pastore N, Magon S. Rehabilitation of endogenous task shift processes in closed head injury patients. Neuropsychol Rehabil 2007;17:1-33.	2+
Working Memory (Individual)	
Westerberg H, Jacobaeus H, Hirvikoski T, Clevberger P, Östensson M-L, Bartfai A, et al. Computerized working memory training after stroke - A pilot study. Brain Inj 2007;21: 21-9.	1+
Cicerone KD. Remediation of "working attention" in mild traumatic brain injury. Brain Inj 2002;16:185-95.	2+
Serino A, Ciaramelli E, Santantonio AD, Malagù S, Servadei F, Làdavas E. A pilot study for rehabilitation of central executive deficits after traumatic brain injury. Brain Inj 2007;21:11-9.	2+
Interventions based on strategies	
Fasotti L, Kovacs F, Eling PA, Brouwer WH. Time pressure management as a compensatory strategy training after closed head injury. Neuropsychol Rehabil 2000;10:47-65.	1+
Meta-analysis	
Park NW, Ingles JL. Effectiveness of attention rehabilitation after an acquired brain injury: a meta-analysis. Neuropsychology 2001;15:199-210.	1++
Review	
Rees L, Marshall S, Hartridge C, Mackie D, Weiser M, ERABI Group. Cognitive interventions post acquired brain injury. Brain Inj 2007;21:161-200.	2++
Neuropsychological rehabilitation of neglect disorders	
Visuo-spatial orientation	
Antonucci G, Guariglia C, Judica A, Magnotti L, Paolucci S, Pizzamiglio L, et al. Effectiveness of neglect rehabilitation in a randomized group study. J Clin Exp Neuropsychol 1995;17:383-9.	1++
Paolucci S, Antonucci G, Guariglia C, Magnotti L, Pizzamiglio L, Zoccolotti P. Facilitatory effect of neglect rehabilitation on the recovery of left hemiplegic stroke patients: A cross-over study. J Neurol 1996;243:308-14.	1++
Weinberg J, Diller L, Gordon WA, Gerstman LJ, Lieberman A, Lakin P, et al. Training sensory awareness and spatial organization in people with right brain damage. Arch Phys Med Rehabil 1979;60:491-6.	1+
Gordon WA, Hibbard MR, Egelko S, Diller L, Shaver MS, Lieberman A, et al. Perceptual remediation in patients with right brain damage: a comprehensive program. Arch Phys Med Rehabil 1985;66:353-9.	2++
Pizzamiglio L, Antonucci G, Judica A, Montenero P, Razzano C, Zoccolotti P. Cognitive Rehabilitation of the hemineglect disorder in chronic patient with unilateral right brain damage. J Clin Exp Neuropsychol 1992;14:901-23.	2++
Schindler I, Kerkhoff G, Karnath HO, Keller I, Goldenberg G. Neck muscle vibration induces lasting recovery in spatial neglect. J Neurol Neurosurg Psychiatry 2002;73:412-9.	2++
Young GC, Collins D, Hren M. Effect of pairing scanning training with block design training in the remediation of perceptual problems in left hemiplegics. J Clin Neuropsychol 1983;5:201-12.	2++
Paolucci S, Antonucci G, Grasso MG, Pizzamiglio L. The role of unilateral spatial neglect in rehabilitation of right brain-damaged ischemic stroke patients: a matched comparison. Arch Phys Med Rehabil 2001;82:743-9.	2+
Pizzamiglio L, Fasotti L, Jehkonen M, Antonucci G, Magnotti L, Boelen D, et al. The use of optokinetic stimulation in rehabilitation of the hemineglect disorder. Cortex 2004;40:441-50.	2+
Wiart L, Come AB, Debelleix X, Petit H, Joseph PA, Mazaux JM, et al. Unilateral neglect syndrome rehabilitation by trunk rotation and scanning training. Arch Phys Med Rehabil 1997;78:424-9.	2+
Brunila T, Lincoln N, Lindell A, Tenovuo O, Hamalainen H. Experiences of combined visual training and arm activation in the rehabilitation of unilateral visual neglect: A clinical study. Neuropsychol Rehabil 2002;12:27-40.	3
Kerkhoff G. Rehabilitation of visuospatial cognition and visual exploration in neglect: A cross-over study. Res Neurol Neurosc 1998;12:27-40.	3

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Robertson IH, Gray JM, Pentland B, Waite LJ. Microcomputer-based rehabilitation for unilateral left visual neglect: A randomized controlled trial. Arch Phys Med Rehabil 1990;71:663-8.	3
Vallar G, Guariglia C, Magnotti L, Pizzamiglio L. Dissociation between position sense and visuo-spatial components of hemineglect through a specific rehabilitation treatment. J Clin Exp Neuropsychol 1997;19:763-71.	3
Cherney LR, Halper AS, Papachronis D. Two approaches to treating unilateral neglect after right hemisphere stroke: a preliminary investigation. Top Stroke Rehabil 2003;9:22-33.	4
Prism adaptation	
Frassinetti F, Angeli V, Meneghello F, Avanzi S, Ladavas E. Long-lasting amelioration of visuospatial neglect by prism adaptation. Brain 2002;125:608-23.	2++
Rousseaux M, Bernati T, Saj A, Kozlowski O. Ineffectiveness of prism adaptation on spatial neglect signs. Stroke 2006;37:542-3.	2++
Serino A, Angeli V, Frassinetti F, Ladavas E. Mechanisms underlying neglect recovery after prism adaptation. Neuropsychologia 2006;44:1068-78.	2++
Tilikete C, Rode G, Rossetti Y, Pichon J, Li L, Boisson D. Prism adaptation to rightward optical deviation improves postural imbalance in left-hemiparetic patients. Curr Biol 2001;11:524-8.	2++
Angeli V, Meneghello F, Mattioli F, Ladavas, E. Mechanisms underlying visuo-spatial amelioration of neglect after prism adaptation. Cortex 2004;40:155-6.	2+
Rossetti Y, Rode G, Pisella L, Farne A, Li L, Boisson D, et al. Prism adaptation to a rightward optical deviation rehabilitates left hemispatial neglect. Nature 1998;395:166-9.	2+
Berberovic N, Pisella L, Morris AP, Mattingley JB. Prismatic adaptation reduces biased temporal order judgements in spatial neglect. Neuroreport 2004;15:1199-204.	3
Datié AM, Paysant J, Destainville S, Sagez A, Beis JM, André JM. Eye movements and visuoverbal descriptions exhibit heterogeneous and dissociated patterns before and after prismatic adaptation in unilateral spatial neglect. Eur J Neurol 2006;13:772-9.	3
Dijkerman HC, McIntosh RD, Milner AD, Rossetti Y, Tilikete C, Roberts RC. Ocular scanning and perceptual size distortion in hemispatial neglect: effects of prism adaptation and sequential stimulus presentation. Exp Brain Res 2003;153:220-30.	3
Dijkerman HC, Webeling M, ter Wal JM, Groet E, van Zandvoort MJ. A long-lasting improvement of somatosensory function after prism adaptation, a case study. Neuropsychologia 2004;42:1697-702.	3
Farné A, Rossetti Y, Toniolo S, Ladavas E. Ameliorating neglect with prism adaptation: visuo-manual and visuo-verbal measures. Neuropsychologia 2002;40:718-29.	3
Ferber S, Danckert J, Joanisse M, Goltz HC, Goodale MA. Eye movements tell only half the story. Neurology 2003;60:1826-9.	3
Maravita A, McNeil J, Malhotra P, Greenwood R, Husain M, Driver J. Prism adaptation can improve contralesional tactile perception in neglect. Neurology 2003;60:1829-31.	3
McIntosh RD, Rossetti Y, Milner AD. Prism adaptation improves chronic visual and haptic neglect: a single case study. Cortex 2002;38:309-20.	3
Morris AP, Kritikos A, Berberovic N, Pisella L, Chambers CD, Mattingley JB. Prism adaptation and spatial attention: a study of visual search in normals and patients with unilateral neglect. Cortex 2004;40:703-21.	3
Rode G, Rossetti Y, Boisson D. Prism adaptation improves representational neglect. Neuropsychologia 2001;39:1250-4.	3
Sarri M, Kalra L, Greenwood R, Driver J. Prism adaptation changes perceptual awareness for chimeric visual objects but not for chimeric faces in spatial neglect after right-hemisphere stroke. Neurocase 2006;12:127-35.	3
Serino A, Bonifazi S, Pierfederici L, Ladavas E. Neglect treatment by prism adaptation: What recovers and for how long. Neuropsychol Rehabil 2007;17:657-87.	3
Vallar G, Zilli T, Gandola M, Bottini G. Productive and defective impairments in the neglect syndrome: graphic perseveration, drawing productions and optic prism exposure. Cortex 2006;42:911-20.	3
Keane S, Turner C, Sherrington C, Beard JR. Use of fresnel prism glasses to treat stroke patients with hemispatial neglect. Arch Phys Med Rehabil 2006;86:1668-72.	4
Optokinetic nistagmus	
Pizzamiglio L, Fasotti L, Jehkonen M, Antonucci G, Magnotti L, Boelen D, et al. The use of optokinetic stimulation in rehabilitation of the hemineglect disorder. Cortex 2004;40:441-50.	1+
Bisiach E, Pizzamiglio L, Nico D, Antonucci G. Beyond unilateral neglect. Brain 1996;119:851-7.	2+
Karnath HO. Optokinetic stimulation influences the disturbed perception of body orientation in spatial neglect. J Neurol Neurosurg Psychiatry 1996;60:217-20.	2+

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Kerkhoff G, Schindler I, Keller I, Marquardt C. Visual background motion reduces size distortion in spatial neglect. NeuroReport 1999;10:319-23.	2+
Kerkhoff G. Multiple perceptual distortion and their modulation in leftsided visual neglect. Neuropsychologia 2000;38:1073-86.	2+
Pizzamiglio L, Frasca R, Guariglia C, Incoccia C, Antonucci G. Effect of optokinetic stimulation in patients with visual neglect. Cortex 1990;26:535-40.	2+
Vallar G, Antonucci G, Guariglia C, Pizzamiglio L. Deficits of position sense, unilateral neglect and optokinetic stimulation. Neuropsychologia 1993;31:1191-200.	2+
Vallar G, Guariglia C, Magnotti L, Pizzamiglio L. Optokinetic stimulation affects both vertical and horizontal deficits of position sense in unilateral neglect. Cortex 1995;31:669-83.	2+
Mattingley JB, Bradshaw JL, Bradshaw JA. Horizontal visual motion modulates focal attention in left unilateral spatial neglect. J Neurol Neurosurg Psychiatry 1994;57:1228-35.	3
Caloric vestibular stimulation	
Adair JC, Na DL, Schwartz RL, Heilman KM. Caloric stimulation in neglect: evaluation of response as a function of neglect type. J Int Neuropsychol Soc 2003;9:983-8.	2+
Bottini G, Paulesu E, Gandola M, Loffredo S, Scarpa P, Sterzi R, et al. Left caloric vestibular stimulation ameliorates right hemianesthesia. Neurology 2005;65:1278-83.	2+
Rode G, Tilikete C, Luaute J, Rossetti Y, Vighetto A, Boisson D. Bilateral vestibular stimulation does not improve visual hemineglect. Neuropsychologia 2002;40:1104-6.	3
Transcutaneous electrical stimulation	
Guariglia C, Coriale G, Cosentino T, Pizzamiglio L. TENS modulates spatial reorientation in neglect patients. Neuroreport 2000;11:1945-8.	2+
Johannsen L, Ackermann H, Karnath HO. Lasting amelioration of spatial neglect by treatment with neck muscle vibration even without concurrent training. J Rehabil Med 2003;35:249-53.	2+
Vallar G, Rusconi ML, Barozzi S, Bernardini B, Ovadia D, Papagno C, et al. Improvement of left visuo-spatial hemineglect by left-sided transcutaneous electrical stimulation. Neuropsychologia 1995;33:73-82.	2+
Vallar G, Rusconi ML, Bernardini B. Modulation of neglect hemianesthesia by transcutaneous electrical stimulation. J Int Neuropsychol Soc 1996;2:452-9.	2+
Feedback	
Harvey M, Hood B, North A, Robertson IH. The effects of visuomotor feedback training on the recovery of hemispatial neglect symptoms: assessment of a 2-week and follow-up intervention. Neuropsychologia 2003;41:886-93.	2+
Tham K, Tegner R. Video feedback in the rehabilitation of patients with unilateral neglect. Arch Phys Med Rehab 1997;78:410-3.	2+
Robertson IH, Nico D, Hood BM. Believing what you feel: using proprioceptive feedback to reduce unilateral neglect. Neuropsychology 1997;11:53-8.	3
Eye patch	
Beis JM, André JM, Baumgarten A, Challier B. Eye patching in unilateral spatial neglect: efficacy of two methods. Arch Phys Med Rehabil 1999;80:71-6.	2+
Zeloni G, Farnè A, Baccini M. Viewing less to see better. J Neurol Neurosurg Psychiatry 2002;3:195-8.	2+
Fong KN, Chan MK, Ng PP Tsang MH, Chow KK, Lau CW, et al. The effect of voluntary trunk rotation and half-field eye-patching for patients with unilateral neglect in stroke: a randomized controlled trial. Clin Rehabil 2007;21:729-41.	–
Neuropharmacological treatments	
Grujic Z, Mapstone M, Gitelman DR, Johnson N, Weintraub S, Hays A, et al. Dopamine agonists reorient visual exploration away from the neglected hemispace. Neurology 1998;51:1395-8.	3
Hurford P, Stringer AY, Jann B. Neuropharmacologic treatment of hemineglect: a case report comparing bromocriptine and methylphenidate. Arch Phys Med Rehabil 1998;79:346-9.	3
Barrett AM, Crucian GP, Schwartz RL, Heilman KM. Adverse effect of dopamine agonist therapy in a patient with motor-intentional neglect. Arch Phys Med Rehabil 1999;80:600-3.	3

Reference	Level of evidence
Neuropsychological rehabilitation of acquired dysexecutive disorders	
Page maker	
Wilson BA, Emslie HC, Quirk K, Evans JJ. Reducing everyday memory and planning problems by means of a paging system: a randomised control crossover study. J Neurol Neurosurg Psychiatry 2001;70:477-82.	1++
Goal management therapy (single session)	
Levine B, Robertson IH, Clare L, Carter G, Hong J, Wilson BA, et al. Rehabilitation of executive functioning: An experimental-clinical validation of goal management training. J Int Neuropsychol Soc 2000;6:299-312.	1+
Goal planning – individual or group training	
Powell J, Heslin J, Greenwood R. Community based rehabilitation after severe traumatic brain injury: a randomised controlled trial. J Neurol Neurosurg Psychiatry 2002;72:193-202.	1+
Problem solving therapy (with or without PC)	
Soong W, Tam SS, Man WK, Hui-Chan C. A pilot study on the effectiveness of tele-analogy-based problem-solving training for people with brain injuries. Int J Rehabil Res 2005;28:341-7.	2++
Social communication – Individual training	
Dahlberg CA, Cusick CP, Hawley LA, Newman JK, Morey CE, Harrison-Felix CL, et al. Treatment efficacy of social communication skills training after traumatic brain injury: a randomized treatment and deferred treatment controlled trial. Arch Phys Med Rehabil 2007;88:1561-73.	2+
Time organization – Individual training	
Fish J, Evans JJ, Nimmob M, Martin E, Kersel D, Bateman A, et al. Rehabilitation of executive dysfunction following brain injury: "Content-free" cueing improves everyday prospective memory performance. Neuropsychologia 2007;45:1318-30.	2+
Social skill training	
Hashimoto K, Okamoto T, Watanabe S, Ohashi M. Effectiveness of a comprehensive day treatment program for rehabilitation of patients with acquired brain injury in Japan. J Rehabil Med 2006;38:20-5.	2+
Autobiography recall (single session)	
Hewitt J, Evans JJ, Dritschel B. Theory driven rehabilitation of executive functioning: Improving planning skills in people with traumatic brain injury through the use of an autobiographical episodic memory cueing procedure. Neuropsychologia 2006;44:1468-74.	2+
Periodic alerting signal	
Manly T, Hawkins K, Evans J, Woldt K, Robertson IH. Rehabilitation of executive function: facilitation of effective goal management on complex tasks using periodic auditory alerts. Neuropsychologia 2002;40:271-81.	2+
Problem solving therapy	
Rath JF, Simon D, Langenbahn DM, Sherr RL, Diller L. Group treatment of problem-solving deficits in outpatients with traumatic brain injury: A randomized outcome study. Neuropsychol Rehabil 2003;13:461-88.	2+
Categorization (abstract thinking)	
Constantinidou F, Thomas RD, Scharp VL, Laske KM, Hammerly MD, Guitonde S. Effects of categorization training in patients with TBI during postacute rehabilitation: preliminary findings. J Head Trauma Rehabil 2005;20:143-57.	3
Specific training (internet)	
Egan J, Worrall L, Oxenham D. An Internet training intervention for people with traumatic brain injury: barriers and outcomes. Brain Inj 2005;19:555-68.	3
Specific training (kitchen)	
Zhang L, Abreu BC, Seale GS, Masel B, Christiansen CH, Ottenbacher KJ. A virtual reality environment for evaluation of a daily living skill in brain injury rehabilitation: reliability and validity. Arch Phys Med Rehabil 2003;84:1118-24.	3
Interactive strategy modeling	
Marshall RC, Karow CM, Morelli CA, Iden KK, Dixon J, Cranfill TB. Effects of interactive strategy modelling training on problem-solving by persons with traumatic brain injury. Aphasiology 2004;18:659-73.	3
Planning training – at home	
Palmisano B, Arco L. Changes in functional behaviour of adults with brain injury and spouse-caregiver burden with in-home neurobehavioural intervention. Behav Change 2007;24:36-49.	3
Specific training (writing notes)	
Turkstra LS, Flora TL. Compensating for executive function impairments after TBI: a single case study of functional intervention. J Commun Disord 2002;35:467-82.	3

Reference	Level of evidence
Goal planning approach	
Wilson BA, Evans JJ, Keohane C. Cognitive rehabilitation: a goal-planning approach. J Head Trauma Rehabil 2002;17:542–55.	3
Neuropsychological rehabilitation of patients with mild traumatic brain injury (TBI)	
Neuropsychological rehabilitation of patients with mild TBI	
Elgmark Andersson E, Emanuelson I, Bjorklund R, Stalhammar DA. Mild traumatic brain injuries: The impact of early intervention on late sequelae. A randomized controlled trial. Acta Neurochirur 2007;149:151-9.	1+
Schoenberger NE, Shif SC, Esty ML, Ochs L, Matheis RJ. Flexyx neurotherapy system in the treatment of traumatic brain injury: An initial evaluation. J Head Trauma Rehabil 2001;16:260-74.	1+
Andary MT, Crewe N, Ganzel SK, Haines-Pepi C, Kulkarni MR, Stanton DF, et al. Traumatic brain injury/chronic pain syndrome: A case comparison study. Clin J Pain 1997;13:244-50.	2-
Cicerone KD, Smith LC, Ellmo W, Mangel HR. Neuropsychological rehabilitation of mild traumatic brain injury. Brain Inj 1996;10:277-86.	2-
Ho MR, Bennett TL. Efficacy of neuropsychological rehabilitation for mild-moderate traumatic brain injury. Arch Clin Neuropsychol 1997;12:1-11.	2-
Laatsch LK, Thulborn KR, Krisky CM, Shobat DM, Sweeney JA. Investigating the neurobiological basis of cognitive rehabilitation therapy with fMRI. Brain Inj 2004;18:957-74.	2-
Tinius TP, Tinius KA. Changes after EEG biofeedback and cognitive retraining in adults with mild traumatic brain injury and attention deficit hyperactivity disorder. Journal of Neurotherapy 2000;4:27-44.	2-
Byers AP. Neurofeedback therapy for a mild head injury. J Neurother 1995;1:22-37.	3
Musiek FE, Baran JA, Shinn J. Assessment and remediation of an auditory processing disorder associated with head trauma. J Am Acad Audiol 2004;15:117-32.	3
Neuropsychological rehabilitation of mixed groups including mild TBI	
Gray JM, Robertson I, Pentland B, Anderson S. Microcomputer-based attentional retraining after brain damage: A randomised group controlled trial. Neuropsychol Rehabil 1992;2:97-115.	1+
Relander M, Troupp H, Bjorkesten G. Controlled trial of treatment for cerebral concussion. Br Med J 1972;4:777-9.	1+
Goranson TE, Graves RE, Allison D, La Freniere R. Community integration following multidisciplinary rehabilitation for traumatic brain injury. Brain Inj 2003; 17:759-74.	2+
Sander AM, Roebuck TM, Struchen MA, Sherer M, High WM, Jr. Long-term maintenance of gains obtained in postacute rehabilitation by persons with traumatic brain injury. J Head Trauma Rehabil 2001;16:356-73.	2-
Holistic rehabilitation in patients with mild TBI	
Ghaffar O, McCullagh S, Ouchterlony D, Feinstein A. Randomized treatment trial in mild traumatic brain injury. Journal of Psychosomatic Research 2006;61:153-60.	1+
Malec JF, Smigielski JS, DePompolo RW, Thomson JM. Outcome evaluation and prediction in a comprehensive-integrated post-acute outpatient brain injury rehabilitation programme. Brain Inj 1993;7:15-29.	2+
Malec JF. Impact of comprehensive day treatment on societal participation for persons with acquired brain injury. Arch Phys Med Rehabil 2001;82:885-95.	2+
Prigatano GP, Fordyce DJ, Zeiner HK, Roueche JR, Pepping M, Wood BC. Neuropsychological rehabilitation after closed head injury in young adults. J Neurol Neurosurg Psychiatry 1984;47:505-13.	2+
Rattok J, Ben-Yishay Y, Ezrachi O, Lakin P, Piasetsky E, Ross B, et al. Outcome of different treatment mixes in a multidimensional neuropsychological rehabilitation. Neuropsychology 1992;6:395-415.	2+
Education programmes for patients with mild TBI and caregivers	
Wade DT, King NS, Wenden FJ, Crawford S, Caldwell FE. Routine follow-up after head injury: A second randomized controlled trial. J Neurol Neurosurg Psychiatry 1998;65:177-83.	1+
Mittenberg W, Tremont G, Zielinski RE, Fichera S, Rayls KR. Cognitive-Behavioral Prevention of Postconcussion Syndrome. Arch of Clin Neuropsychology 1996;2:139-45.	1+
Paniak C, Toller-Lobe G, Durand A, Nagy J. A randomized trial of two treatments for mild traumatic brain injury. Brain Inj 1998;12:1011-23.	1+
Paniak C, Toller-Lobe G, Reynolds S, Melnyk A, Nagy J. A randomized trial of two treatments for mild traumatic brain injury: 1 year follow-up. Brain Inj 2000;14: 219-26.	1+
Ponsford J, Willmott C, Rothwell A, Cameron P, Kelly A-M, Nelms R, et al. Impact of early intervention on outcome following mild head injury in adults. J Neurol Neurosurg Psychiatry 2002;73:330-2.	1+